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Use of contraceptives in cats with ovarian and uterine pathology

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Abstract. Regulation of the reproductive capacity of cats using megestrol acetate (a gestagenic preparation) contributes to the improvement of pathological processes in the uterus, ovaries, and imbalance of gonadal hormones. Therefore, it is essential to investigate and scientifically substantiate the pathomorphological processes in the body of cats under medical contraception. The purpose of this study was to substantiate the pathomorphological changes and dynamics of certain blood parameters in the body of cats under the use of megestrol acetate. The study employed clinical (examination,

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palpation), laboratory (haematological, biochemical, hormonal), morphological (examination of the genital organs of cats, computed during ovariohysterectomy) methods. A decrease in ovarian size in hypotrophic cats by $11.3 \times 9.05\%$ was found compared to the ovaries of healthy cats. The dependence of megestrol acetate administration on the occurrence of cystic formations in the ovaries was found, with an increase in ovaries in the experimental group by 1.2×2.4 times in follicular cysts and by 1.9×3.1 and 2.5×3.9 times in luteal cysts and polycystic cysts, respectively. It was found that the uterus in cats with megestrol acetate was increased by 3.16×1.93 times in the right horn and 2.84×1 times in the left horn compared to the uterus of healthy cats. The dynamics of progesterone (increase by 37.85%), follicle-stimulating hormone (decrease by 43.75%) and oestradiol (increase by 72.15%) were determined in comparison with intact animals. The increase in serum glucose levels in cats after megestrol administration by 34.31% , total protein by 25.0% and creatinine by 11.10% , aspartate aminotransferase by 43.84% (1.78 times) and alanine aminotransferase by 49.84% (1.99 times), and serum urea by 58.71% was substantiated. At the same time, haemoglobin levels decreased by 16.5% . The findings of this study can be used in the development of new methods and regimes of medical contraception with minimisation of risks of complications of the reproductive system, regulation of reproductive capacity, and prevention of infertility in cats.

Keywords: contraceptive agents; megestrol acetate; cysts; pyometra; endometritis

INTRODUCTION

The use of megestrol acetate-based drugs to correct sexual cyclicity in cats is widely used by pet owners. This leads to an increase in the number of gynaecological pathologies due to an imbalance of sex hormones. Uncontrolled use of megestrol acetate to interrupt sexual desire in cats causes both functional disorders of the reproductive system (hypotrophy and ovarian cysts) and inflammatory processes (metritis and pyometra). The scientific and practical substantiation of the negative impact of megestrol acetate will make it possible to prevent the occurrence of gynaecological pathology in cats.

The use of progestogenic contraceptives to prevent heat in cats with a 1-year interval leads to destructive changes in the genitals. S.S. Goericke-Pesch (2017) claims that after discontinuation of megestrol acetate-based preparations, fertility is restored. However, O.I. Shkromada and A.V. Rokochoyi (2023) obtained data that the manifestation of gynaecological pathology in cats occurs due to the improper use of megestrol acetate-based preparations. This is what initially leads to disruption of the sexual cycles of cats, as noted by O. Burlakova and V. Stefanyk (2021), and subsequently to pathological inflammatory processes in the organs of the reproductive system: pyometra, endometritis. Furthermore, Z. Niewiadomska *et al.* (2023) point to the development of histological endometrial hyperplasia after the use of a megestrol acetate-based preparation, which further interferes with the physiological development of the placenta and contributes to early and subclinical abortions caused by impaired embryo implantation. G. Martini *et al.* (2023) point to the development of pyometra as a consequence of the increase in oestradiol $17\text{-}\beta$ content provoked by the use of megestrol acetate.

Therewith, R. Hagman (2022) notes the development of pyometra in cats as a consequence of hormone levels, specifically oestrogen and progesterone, during 4 months, which, according to C.V. Lindsay *et al.* (2023), is the cause of infertility in cats and is caused by

the prolonged use of megestrol acetate. In addition, C. Binder *et al.* (2021) pointed out the key role of progesterone block in the early stages of pregnancy in cats, noting that when progesterone levels decrease, either a habitual abortion or partial or complete foetal resorption occurs. S. Romagnoli and L. Ferre-Dolcet (2022) claim that the use of megestrol acetate-based preparations every 13 weeks can prevent ovulation, and longer-term use provokes the development of hypersecretory nodules and neoplastic areas in the mammary gland. In addition, S. Chotimanukul *et al.* (2023) notes that ovulation occurs at a 2:1 ratio of follicle-stimulating to luteinising hormone.

According to J. Liang *et al.* (2023), pathology of the ovaries and uterus in cats is quite common. As noted by A. Fonthonne *et al.* (2020), the most common pathological conditions are ovarian hypotrophy, ovarian cysts, and uterine inflammation. H. Moosavian *et al.* (2022) point out that the problem of feline reproduction has many issues that require a thorough analysis, namely: how to safely use medical contraceptives to prevent ovulation with the subsequent restoration of the fertility of cats, e.g., when resting between pregnancies in pedigree cats; what consequences can be expected when using megestrol acetate-based gestational agents and how to prevent them. E.A. McGlade *et al.* (2022) state that increased progesterone contributes to a decrease in local (tissue) defence responses and a decrease in the count of saprophytic (*Lactobacilli*) bacteria in the vagina of cats, which contributes to an increase in the count of opportunistic pathogens such as streptococci and staphylococci, which subsequently provoke the development of endometritis.

Despite the considerable number of publications, the issue of using oestrus inhibitors in cats stays relevant for many areas of veterinary medicine, specifically reproductive medicine – for the development of technological schemes in the professional breeding of purebred

animals, surgery – for the creation of surgery protocols for the treatment of detected pathologies and risk reduction after surgery. This issue is also relevant in wartime. After all, in the current conditions in Ukraine, there is an acute problem of uncontrolled reproduction of abandoned and stray animals, hence the spread of dangerous infections in the absence of veterinary services for neutering dogs and cats and vaccination. Therefore, in dangerous and uncontrolled areas, alternative schemes should be sought to control animal reproduction with medicated contraception with minimal risk to animal health. That is why the purpose of the study was to establish and scientifically substantiate changes in the organs of the reproductive system of cats when using megestrol acetate-based preparations.

MATERIALS AND METHODS

The study was conducted in the clinical and diagnostic advisory centre "Vet camp" of the Faculty of Veterinary Medicine of Sumy National Agrarian University during 2023. The study was conducted in 2 stages. At the first stage, 2 groups of cats were formed: 1) control (no megestrol acetate was used), 2) experimental (megestrol acetate was used according to the guidelines). There were 15 animals in each group. Therewith, the prevalence of gynaecological pathology, morphological characteristics of the ovaries and uterus, and the dynamics of progesterone, oestradiol, and follicle-stimulating hormone were determined. Morphometric parameters and cysts of the ovaries and uterus were examined after ovariectomy according to the generally accepted method of S. Bowen *et al.* (2007), according to which the normal size of the ovaries in cats is 10×6×4 mm. The concentration of progesterone, follicle-stimulating hormone and progesterone was determined using an ImmunoChem-2100 analyser (USA) according to the instructions. The obtained digital material was processed according to the methods of variation statistics using SPSS Data editor 17.0 version.

At the second stage, 30 experimental animals were divided into 2 groups based on the principle of analogues, with 15 cats in each group. The cats were divided according to the history of contraceptive use; the first group did not use such preparations, and the second group used preparations with the active ingredient megestrol acetate. Therewith, Group 1 was control (cats without signs of inflammatory processes in the reproductive system) and Group 2 was experimental (cats with signs of endometritis). Upon the study of blood serum of both groups of cats, the content of basic biochemical parameters such as glucose, haemoglobin, total protein, creatinine, aspartate aminotransferase, alanine aminotransferase, and urea were determined.

For the study of haematological parameters (number of red blood cells and white blood cells) and determination of hormonal status, blood was taken from the saphenous veins of the forearm or thigh, depending on the degree of their filling, using tubes with a blood clotting activator for biochemical studies and an anticoagulant ethylenediaminetetraacetate (EDTA K3) for clinical studies. Blood tests were performed using a semi-automatic analyser Mindray BA-88 (biochemical analysis) (China) and an automatic haematological analyser H360 (clinical analysis) (Erba Lachema s.r.o., Czech Republic). Animals were kept and all manipulations were carried out according to the Law of Ukraine No. 249 "Procedure for Conducting Research and Experiments on Animals by Scientific Institutions" (2012), European Convention for the Protection of Vertebrate Animals (1986).

RESULTS AND DISCUSSION

Analysing the prevalence of ovarian pathologies, it was found that in the group where megestrol acetate was used, ovarian hypotrophy was diagnosed 3 times less frequently, which is associated with a violation of the rhythmicity of the cyclic peaks of the main sex hormones (Table 1).

Table 1. Prevalence of ovarian and uterine pathologies in cats depending on the use of contraceptives

Indicator	Group 1 – control (n=15)	Group 2 – with the use of megestrol acetate (n=15)
Ovarian hypotrophy	1	3
Follicular cyst	–	2
Luteal cyst	–	1
Polycystic disease	–	5
Pyometra	2	2
Endometritis	1	2

Source: compiled by the authors of this study

Follicular (n=2), luteal (n=1) and polycystic (n=1) cysts in cats were diagnosed only in the group treated with megestrol acetate, which emerged on the background of systematic disorders of sexual cycles, which led to a violation of the hormonal status of sex hormones and

the transformation of follicles into cysts. The morphological characteristics of the ovaries and uterus in cats of the experimental groups differed and caused different parameters in the diagnosis and development of preventive measures (Table 2).

Table 2. Morphological characteristics of the ovaries and uterus

Indicator	Group 1 – control (n=15)		Group 2 – with the use of megestrol acetate (n=15)	
	right	left	right	left
ovary, hypotrophy				
Longitudinal diameter, cm	–	0.41	0.43±0.03	0.42±0.04
Transverse diameter, cm	–	0.22	0.21±0.02	0.25±0.03
ovary, follicular cyst				
Longitudinal diameter, cm	–	–	0.91±0.01	0.93±0.02
Transverse diameter, cm	–	–	0.52±0.03	0.56±0.01
ovary, luteal cyst				
Longitudinal diameter, cm	–	–	1.1±0.05	1.2±0.03
Transverse diameter, cm	–	–	0.61±0.04	0.65±0.06
ovary, polycystic disease				
Longitudinal diameter, cm	–	–	1.4±0.07	1.6±0.08
Transverse diameter, cm	–	–	0.82±0.09	0.73±0.07
uterus, pyometra				
	right horn	left horn	right horn	left horn
Length, cm	10.3±0.36	7.0±0.47	11.36±1.2	10.5±1.1
Transverse diameter, cm	2.6±0.02	2.7±0.5	3.1±0.1	3.3±0.1
uterus, endometritis				
Length, cm	5.1	5.0	6.3±1.2	6.1±0.94
Transverse diameter, cm	1.1	1.2	0.97±0.06	0.87±0.12

Source: compiled by the authors of this study

In hypotrophy, the ovaries of cats of both groups were reduced, and therefore, the size of the ovary in the first group was 0.41×0.21 cm, while in cats of the Group 2 the size ranged from 0.42±0.04×0.25±0.03 – left to 0.43±0.03×0.21±0.02 cm – right. This is caused by excessively high levels of progestogen in the blood of cats, which blocks the formation of follicle-stimulating and luteinising hormones by blocking the release of releasing hormone. The conclusions coincide with those drawn by E.R.S. Maylem and L.J. Spicer (2022).

It was found that the occurrence of such pathologies as follicular and luteal cysts and polycystic ovaries is more correlated with the use of megestrol acetate. Thus, the development of cystic degeneration in cats that did not take megestrol acetate was not found. At the same time, in cats of the Group 2, the size of the ovaries in follicular cysts ranged from 0.91±0.01×0.52±0.03 to 0.93±0.02×0.56±0.01 cm, which is 1.7×2.47 times larger than in healthy cats (p<0.05). A comparable trend was observed in animals with luteal cysts and polycystic disease. The size of the ovary in cats with luteal cysts was 1.9×3.1 times (p<0.001) and in polycystic cysts – 2.5×3.9 times (p<0.001) greater than in healthy animals. The

formation of cysts is triggered by an imbalance of follicle-stimulating and luteinising hormones.

In the presence of the influence of megestrol acetate, the release of releasing hormone is inhibited, which stimulates the formation of follicle-stimulating and luteinising hormones. In this case, releasing hormone has an α-isomer that promotes the formation of follicle-stimulating hormone and a β-isomer that affects the amount of luteinising hormone formation. Therefore, inhibition of the α-isomer of releasing hormone creates conditions for the development of luteal cysts, and reduction of the β-isomer creates conditions for the development of follicular cysts.

Pyometra is characterised by purulent inflammation of all layers of the uterus. Therewith, the size of the uterus increases significantly, it becomes pain-inducing and blood-filled. The uterus was found to be enlarged during pyometra in cats of Group 1 by 1.7×1.7 times (p<0.001) in the right horn (Fig. 1a) and 1.94×1.69 (p<0.001) in the left horn and cats of Group 2 – by 3.16×1.93 times (p<0.001) in the right horn and 2.84×2.1 (p<0.001) times in the left horn (Fig. 1b).

The use of contraceptives, specifically megestrol acetate, is based on changes in the content of sex hormones and their ratios (Table 3)

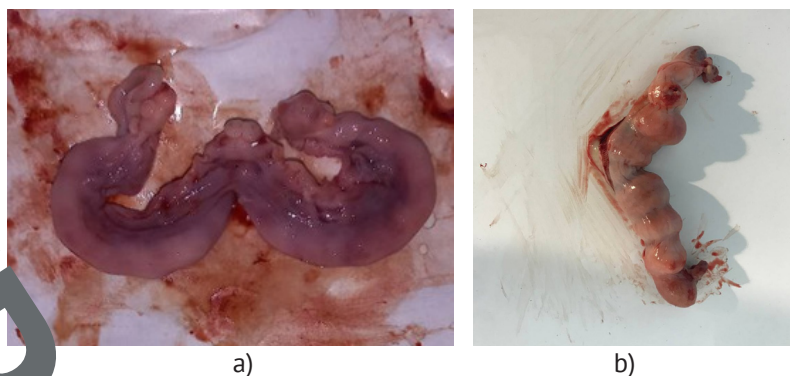


Figure 1. Feline uterus with pyometry

Notes: a) Uterus of a Group 1 cat with pyometry; b) Uterus of a Group 2 cat with pyometry

Table 3. Progesterone, oestradiol, and follicle-stimulating hormone levels ($M \pm m$)

Indicator	Group 1 – control (n=15)	Group 2 – with the use of megestrol acetate (n=15)
Progesterone, ng/ml	13.5±0.26	21.72±0.16
Oestradiol, pg/ml	61.11±5.37	105.2±1.97
Follicle-stimulating hormone, UI/l	0.16±0.045	0.09±0.008

Source: compiled by the authors of this study

It was found that the progesterone content in the blood serum of cats treated with megestrol acetate increased by 37.85% (1.61 times), oestradiol – by 72.15% (1.72 times), and follicle-stimulating hormone decreased by 43.75% (1.78 times). Therewith, cases of follicular cysts formation were diagnosed in cats of Group 2, which was caused by an imbalance of sex hormones, namely, high (0.16±0.05 UI/l) follicle-stimulating hormone. This is also confirmed by an increase in the ratio of progesterone to oestradiol. Thus, the ratio

of progesterone to oestradiol in Group 1 was 4.5, while in Group 2, where megestrol acetate was used, this ratio was 4.84, which is 6.54% (1.07 times higher). Changes in the main biochemical parameters that are markers of homeostasis disorders, specifically the development of subclinical or chronic inflammatory processes, which subsequently lead to endometritis or pyometra, which in turn lead to persistent infertility of cats and the emergence of various pathologies of the reproductive system (Table 4).

Table 4. Dynamics of the main biochemical parameters

Indicator	Group 1 – control group (n=15)	Group 2 – with the use of megestrol acetate (n=15)
Glucose, mmol/l	4.48±0.12	6.82±0.16
Haemoglobin, g/l	90.25±3.47	75.36±0.32
Total protein, g/l	62.97±3.57	83.97±5.67
Creatinine, µmol/l	154.36±6.78	173.64±9.59
Aspartate aminotransferase, IU/l	18.91±1.37	33.64±2.53
Alate aminotransferase, UI/l	41.33±2.61	82.39±3.54
Urea, µmol/l	7.65±0.64	25.82±0.22

Source: compiled by the authors of this study

An increase in serum glucose levels in the megestrol-treated group by 34.31% (1.52 times) was found, which may indicate a compensated insufficiency of insulin content. At the same time, there was a decrease in haemoglobin levels by 16.5% (1.2 times). Therewith, the amount of total protein and creatinine increased by 25.0% (1.33 times) and 11.10% (1.12 times), indicating the development of subclinical inflammatory processes.

There was also an increase in liver enzymes: aspartate aminotransferase (AST) by 43.8% (1.78 times) and alanine aminotransferase (ALT) by 49.84% (1.99 times), serum urea by 58.71% (1.59 times), which also indicates the development of inflammatory processes. It is known that rapid changes in sex hormone levels cause changes in the dynamics of haematological parameters (Table 5).

Table 5. Dynamics of the main haematological parameters during the use of megestrol acetate

Indicator	Group 1 – control (n=15)	Group 2 – with the use of megestrol acetate (n=15)
Red blood cells, t/l	7.21±0.33	4.82±0.38
White blood cells, g/l	17.22±1.92	19.37±4.21
Banded, %	1.1±0.15	3.22±0.24
Segmented, %	43.22±3.29	54.91±4.65
Metamyelocytes, %	0.22±0.01	0.41±0.11

Source: compiled by the authors of this study

A 33.15% (1.51 times) decrease in the count of red blood cells was found with megestrol acetate, while the count of leukocytes, especially different types of neutrophils, tended to increase and change their ratio. Thus, the total number of leukocytes increased by 12.49% (1.12 times) after megestrol acetate administration. Therewith, the percentage of banded neutrophils

increased by 192.73% (2.93 times), segmented neutrophils – by 27.05% (1.27 times), and metamyelocytes – by 86.36% (1.86 times).

The next stage of the study was to determine changes in the main biochemical parameters of the blood of cats with endometritis after the use of megestrol acetate (Table 6).

Table 6. Dynamics of the main biochemical parameters of the blood of cats with endometritis

Indicator	Group 1 – control (n=15)	Group 2 – with the use of megestrol acetate (n=15)
Glucose, mmol/l	4.48±0.12	8.24±0.22*
Haemoglobin, g/l	117.4±3.47	73.64±4.91
Total protein, g/l	62.97±3.57	81.33±4.29
Creatinine, µmol/l	15.37±6.78	192.61±7.02
AST, IU/l	18.91±1.11	62.27±3.32
ALT, IU/l	41.1±2.61	138.22±5.66
Urea, µmol/l	7.1±0.64	22.33±1.48

Source: compiled by the authors of this study

There was a significant increase in glucose by 83.93% (1.84 times), total protein by 29.16% (1.29 times), creatinine by 24.78% (1.25 times), AST by 229% (3.29 times), ALT by 234% (3.34 times), and urea by 191% (2.92 times). At the same time, the haemoglobin level tended to decrease, amounting to 18.40% (1.23 times). Therewith, comparing analogous biochemical parameters of the blood of animals that did not have inflammatory processes (endometritis) of the reproductive system (Table 4), the study found a tendency

to increase glucose levels by 20.82% (1.21 times), creatinine by 10.92% (1.11 times) and a significant increase in AST by 85.11% (1.85 times), ALT by 67.76% (1.68 times), and urea by 363.28% (4.63 times). This change is caused by the development of inflammatory processes against the background of an increase in progesterone levels by 7.85% compared to intact animals. Significant changes in the morphological parameters of blood in the manifestation of endometritis in cats after the use of megestrol acetate were found (Table 7).

Table 7. Dynamics of the main haematological parameters of blood in cats with endometritis

Indicator	Group 1 – control (n=15)	Group 2 – with the use of megestrol acetate (n=15)
Red blood cells, t/l	7.21±0.33	4.82±0.38
White blood cells, g/l	17.22±1.92	23.22±2.6
Banded, %	0.22±0.01	0.41±1.02
Segmented, %	43.22±3.29	64.51±2.7
Metamyelocytes, %	1.1±0.15	0.75±0.11

Source: compiled by the authors of this study

Thus, the count of red blood cells decreased by 33.29% (1.5 times) compared to intact cats. Therewith, the count of leukocytes increased by 34.84%

(1.35 times), including the count of banded neutrophils by 755.45% (8.55 times), segmented neutrophils – by 48% (1.49 times) and metamyelocytes – by 231.82%

times). It is also important to compare analogous blood parameters in cats treated with megestrol acetate with and without endometritis (Table 5). Thus, the count of the red blood cells was not statistically different, but the count of leucocytes in the blood of cats with endometritis was 12.8% higher (1.2 times), the count of banded neutrophils was 192.24% higher (2.92 times), segmented neutrophils – 17.12% higher (1.17 times), and metamyelocytes – 105% higher (1.78 times).

The use of megestrol acetate in cats to prevent signs of heat increases the incidence of gynaecological pathology such as ovarian atrophy and cysts, endometritis, and pyometra. Therewith, the content of oestradiol and progesterone increases, while follicle-stimulating hormone decreases. A decrease in glucose, haemoglobin, and urea, and an increase in total protein, creatinine, AST, ALT in the blood of cats treated with megestrol acetate were also found.

The use of contraceptives that contain substances that affect the course of the sexual cycle of cats by changing the synthesis of both hypothalamic-pituitary hormones and sex hormones, specifically megestrol acetate, contributes to the more frequent manifestation of pathologies such as ovarian hypofunction, follicular cysts, luteal cysts, and polycystic disease, which is also confirmed by publications by foreign authors (Brändli *et al.*, 2021). Particular attention should be paid to the manifestation of pyometra and endometritis after megestrol acetate use. An increase in the number of cases of acute inflammatory processes in the organs of the reproductive system of cats, such as endometritis and pyometra, has been established. Thus, S. Romagnoli *et al.* (2023) report a more intense uterine inflammatory process in cats and an increase in the number of complications after systematic use of megestrol acetate, noting that short-term and especially long-term administration of progesterone derivatives disrupts cell receptors in the endometrial epithelium, allowing pathogens to break through this first natural barrier and thus increase the risk of developing pyometra.

The findings of the study by C. Binder *et al.* (2019) confirmed a 1.9×3.1 to 2.5×3.9-fold increase in ovarian size in cystic degeneration, indicating that the incidence increased with the age of the cats and was complicated by purulent endometritis and hyperplastic endometrial lesions. The determining role of persistent corpus luteum in the development of cystic degeneration was also noted. Therewith, as noted by L. Schirrer *et al.* (2021), cysts occurred when megestrol acetate was used to prevent sexual desire, and polycystic disease occurred when sexual desire was interrupted, which is fully consistent with the findings of the present study. Data were also obtained on the formation of both follicular and luteal cysts in cats treated with megestrol acetate. The reason for this phenomenon is the dysfunction of the hypothalamic and pituitary hormones. H.J.J. Kim *et al.* (2023) indicate that the use of contraceptives disrupts the

functioning of cannabinoid receptors, which is characterised by changes in their expression in relation to oestrogen and progesterone, which coincides with the data obtained. At the same time, the development of luteal cysts is triggered by a violation of follicle-stimulating hormone production or an increase in luteinising hormone secretion (Xia *et al.*, 2020).

Research found destructive changes in the uterine mucosa, manifested in the form of endometritis and pyometra in cats previously treated with megestrol acetate to suppress reproductive capacity. Violation of oestrogen synthesis is accompanied by pathological processes in the organs of the reproductive system. Z. Niewiadomska *et al.* (2023) note that most cases of infertility in cats after megestrol acetate administration are caused by hyperplastic endometrial degeneration, which prevents embryo implantation and placental development.

Data was obtained on the increase in serum glucose by 34.31%, total protein by 11.10%, and creatinine by 25.0% in cats treated with megestrol acetate, which coincides with the opinion of R. Hagman (2018), who notes that pyometra, which develops within 4 months after oestrus or contraceptive use, is caused by the influence of microflora, in the development of which high progesterone levels play a leading role. At the same time, pyometra and endometritis complications are reported in cats older than 5-7 years. The use of megestrol acetate has a negative impact on the reproductive capacity of cats, creating conditions for the formation of ovarian cysts, development of endometritis and pyometra, accompanied by hypertrophic degeneration of the endometrium, and disruption of the main indicators of haemostasis.

CONCLUSIONS

The study substantiated the negative effect of megestrol acetate on the reproductive system of cats and revealed morphological changes in the ovaries and uterus, as well as complications in the form of endometritis and pyometra, which was confirmed by haematological and biochemical blood tests. An increase in the manifestation of ovarian hypofunction by 333.33%, endometritis by 100.0% in cats treated with megestrol acetate compared to intact animals and the occurrence of follicular cysts and pyometra in 13.33% of polycystic disease – 30.0% of the total number of affected cats, indicating the systemic nature of the effect of megestrol acetate on both the organs of the reproductive system and the body of cats as a whole. The study found an increase in the size of ovaries and polycystic ovaries by 2.5×3.9 times, in luteal cysts – by 1.9×3.1 times, and in follicular cysts – by 1.7×2.47 times compared to the ovaries of healthy cats, which may indicate destructive changes in the form of accelerated apoptosis and necrotic processes in the reproductive system. An increase in the progesterone content in the blood serum of cats

with megestrol acetate by 37.85%, oestradiol – by 72.15%, follicle-stimulating hormone – by 43.75% change. It is possible that there are persistent irreversible changes in the secretory capacity of the feline body, which leads to a violation of both the general reproductive capacity and the rhythm of sexual cycles specifically.

Analysis of biochemical parameters, the study found a decrease in haemoglobin levels by 16.5% and an increase in glucose level – by 11%, total protein – by 25.0%, creatinine – by 10%, AST – by 43.84%, ALT – by 49.84%, and serum urea – by 58.71%, which also indicates the development of inflammatory processes in cats after prolonged use of megestrol acetate, indicating a violation of biochemical processes, inherent in the onset of oxidative stress, and the toxic effects of the contraceptive on the feline body. A decrease in the count of red blood cells by 16.5% was recorded with the use of megestrol acetate, while the count of

leukocytes increased by 12.49%, the percentage of banded neutrophils increased by 192.73%, segmented neutrophils – by 27.05%, and metamyelocytes – by 86.36%, which suggests the development of inflammatory processes, such as endometritis and pyometra, specifically, which have an acute course and are accompanied by erythropoiesis disorders and an increase in the white blood cell fraction. In the future, it is planned to investigate cytological changes in the tissues of the reproductive system organs and develop methods for diagnosing and preventing the development of pathologies of the reproductive organs of cats.

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CONFLICT OF INTEREST

The authors of this study declare no conflict of interest.

REFERENCES

- [1] Binder, C., Aurich, C., Reifinger, M., & Aurich, J. (2019). Spontaneous ovulation in cats-uterine findings and correlations with animal weight and age. *Animal Reproduction Science*, 209, article number 106167. doi: [10.1016/j.anireprosci.2019.106167](https://doi.org/10.1016/j.anireprosci.2019.106167).
- [2] Binder, C., Reifinger, M., Aurich, J., & Aurich, J. (2021). Histopathological findings in the uteri and ovaries of clinically healthy cats presented for estrus spaying. *Journal of Feline Medicine and Surgery*, 23(8), 770-776. doi: [10.1177/1098612X20975376](https://doi.org/10.1177/1098612X20975376).
- [3] Bowen, S., Norian, J., Santoro, N., & Hill, L. (2007). Simple tools for assessment of ovarian reserve (OR): Individual ovarian dimensions are reliable predictors of OR. *Fertility and Sterility*, 88(2), 390-395. doi: [10.1016/j.fertnstert.2006.11.175](https://doi.org/10.1016/j.fertnstert.2006.11.175).
- [4] Brändli, S., Palm, J., Kowalewski, M., & Reichler, M. (2021). Long-term effect of repeated deslorelin acetate treatment in bitches for reproduction control. *Theriogenology*, 158, 73-82. doi: [10.1016/j.theriogenology.2021.07.015](https://doi.org/10.1016/j.theriogenology.2021.07.015).
- [5] Burlakova, O., & Stefanyk, V. (2021). Sexual cycle of cats and non-invasive diagnostic methods. *Scientific Messenger of LNU of Veterinary Medicine and Biotechnologies. Series: Veterinary Sciences*, 23(101), 124-132. doi: [10.32718/nvlvet10120](https://doi.org/10.32718/nvlvet10120).
- [6] Chotimanukul, S., Sandra, G.-P., Junpen, S., Jinda, S., Ekkanot, S., Padet, T., & Suppawiwat, P. (2023). Serum anti-müllerian hormone levels and estrous monitoring of GnRH agonist deslorelin-induced estrus in bitches: A pilot study. *Animals*, 13(2), article number 258. doi: [10.3390/ani13020258](https://doi.org/10.3390/ani13020258).
- [7] European Convention for the Protection of Vertebrate Animals (1986). Retrieved from <https://rm.coe.int/168007a67b>.
- [8] Fontbonne, A., Prochowska, S., & Niewiadomska, Z. (2020). Infertility in brood cats – A review of the potential causes. *Theriogenology*, 158, 339-345. doi: [10.1016/j.theriogenology.2020.09.002](https://doi.org/10.1016/j.theriogenology.2020.09.002).
- [9] Goericke-Pesch, S. (2017). Long-term effects of GnRH agonists on fertility and behaviour. *Reproduction in Domestic Animals*, 52(2), 336-347. doi: [10.1111/rda.12898](https://doi.org/10.1111/rda.12898).
- [10] Hagman, R. (2018). Pyometra in small animals. *The Veterinary clinics of North America. Small Animal Practice*, 48(4), 639-661. doi: [10.1016/j.cvsm.2018.03.001](https://doi.org/10.1016/j.cvsm.2018.03.001).
- [11] Hagman, R. (2022). Pyometra in small animals 2.0. *The Veterinary clinics of North America. Small Animal Practice*, 52(3), 631-657. doi: [10.1016/j.cvsm.2022.01.004](https://doi.org/10.1016/j.cvsm.2022.01.004).
- [12] Kim, H.J., Zagzoog, A., Black, T., Baccetto, S.L., & Laprairie, R.B. (2023). Molecular and cellular mechanisms underlying brain region-specific endocannabinoid system modulation by estradiol across the rodent estrus cycle. *Progress in Molecular Biology and Translational Science*, 195, 27-45. doi: [10.1016/j.pmbts.2022.06.010](https://doi.org/10.1016/j.pmbts.2022.06.010).
- [13] Law of Ukraine No. 249 “Procedure for Conducting Research and Experiments on Animals by Scientific Institutions”. (2012, March). Retrieved from <https://zakon.rada.gov.ua/laws/show/z041112#Text>.
- [14] Liang, J., Gao, Y., Feng, Z., Zhang, B., Na, Z., & Li, D. (2023). Reactive oxygen species and ovarian diseases: Antioxidant strategies. *Redox Biology*, 62, article number 102659. doi: [10.1016/j.redox.2023.102659](https://doi.org/10.1016/j.redox.2023.102659).
- [15] Lindsay, C.V., Potter, J.A., Grimshaw, A.A., Abrahams, V.M., & Tong, M. (2023). Endometrial responses to bacterial and viral infection: A scoping review. *Human Reproduction Update*, 29(5), 675-693. doi: [10.1093/humupd/dmad013](https://doi.org/10.1093/humupd/dmad013).

- Martini, G., Bucci, R., Parrillo, S., Carluccio, A., & Pisu, M.C. (2023). Treatment of a recurrent pyometra by surgical uterine drainage in a main coon cat. *Veterinary Sciences*, 10(1), article number 60. doi: [10.3390/vetsci10010060](https://doi.org/10.3390/vetsci10010060).
- [17] Kelen, F.R.S., & Spicer, L.J. (2022). Effects of transforming growth factor β 1 on steroidogenesis of feline granulosa cells cultured *in vitro*. *Reproduction, Fertility, and Development*, 34(11), 789-797. doi: [10.1071/RD22034](https://doi.org/10.1071/RD22034).
- [18] McGlade, F., Miyamoto, A., & Winuthayanon, W. (2022). Progesterone and inflammatory response in the oviduct during physiological and pathological conditions. *Cells*, 11(7), article number 1075. doi: [10.3390/cells11071075](https://doi.org/10.3390/cells11071075).
- [19] Moosavian, H., Gholabi, R., Pourreza, B., & Darbandsari, M. (2022). Diffuse uterine adenomyosis and bilateral ovarian cysts in a chinchilla cat. *Topics in Companion Animal Medicine*, 49, article number 100663. doi: [10.1016/j.tcam.2022.100663](https://doi.org/10.1016/j.tcam.2022.100663).
- [20] Niewiadomski, Z., Adib-Lesaux, A., Reyes-Gomez, E., Gandoin, C., Bouillin, C., Gaillard, V., & Fontbonne, A. (2023). Uterine issues in infertile queens: Nine cases. *Animal Reproduction Science*, 251, article number 107225. doi: [10.1016/j.anireprosci.2023.107225](https://doi.org/10.1016/j.anireprosci.2023.107225).
- [21] Romagnoli, S., & Ferra-Finchet, L. (2022). Reversible control of reproduction in queens: Mastering the use of reproductive drugs to manipulate cyclicity. *Journal of Feline Medicine and Surgery*, 24(9), 853-870. doi: [10.1177/10986123221122112](https://doi.org/10.1177/10986123221122112).
- [22] Romagnoli, S., Diana, A., Barré-Dolé, L., Fontaine, C., & Milani, C. (2023). Chronic use of deslorelin in dogs: Six cases (2005-2022). *Animals: An Open Access Journal From MDPI*, 13(2), article number 265. doi: [10.3390/ani13020265](https://doi.org/10.3390/ani13020265).
- [23] Schirrer, L., Pablo Jesús, M.-G., & Llobregat, L. (2021). Feline polycystic kidney disease: An update. *Veterinary Sciences*, 8(11), article number 269. doi: [10.3390/vetsci8110269](https://doi.org/10.3390/vetsci8110269).
- [24] Shkromada, O.I., & Rokochoyi, A.V. (2023). Factors in the development of cat infertility. *Bulletin of Sumy National Agrarian University. The Series: Veterinary Medicine*, 4(59), 76-82. doi: [10.32845/bsnau.vet.2022.4.12](https://doi.org/10.32845/bsnau.vet.2022.4.12).
- [25] Xia, Y., Wang, Q., He, X.D., Chen, Y., Ji, G., & Zhang, X.D. (2020). Cloning and expression analysis of the follicle-stimulating hormone receptor (FSHR) gene in the reproductive axis of female yaks (*Bos grunniens*). *Domestic Animal Endocrinology*, 70, article number 106383. doi: [10.1016/j.domaniend.2019.07.011](https://doi.org/10.1016/j.domaniend.2019.07.011).

Застосування протизаплідних засобів кішкам із патологією яєчників та матки**Олександр Миколайович Чекан**

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Анотація. Регуляція репродуктивної здатності кішок використанням мегестролу ацетату (гестагенний препарат) сприяє розвитку патологічних процесів у матці, яєчниках, дисбалансу гонадальних гормонів. Тому важливим є дослідження та наукове обґрунтування патогенетичних процесів в організмі кішок за медикаментозної контрацепції. Метою роботи було обґрунтування патоморфологічних змін та динаміки окремих показників крові в організмі кішок, при застосуванні мегестролу ацетату. Під час проведення досліджень використані клінічні (огляд, пальпація), лабораторні (гематологічні, біохімічні, гормональні), морфологічні (дослідження органів статеві системи кішок, а також вивчення під час оваріогістеректомії) методи. Встановлено зменшення величини яєчників при гіпотрофії кішок на 3×9,05 % порівняно із яєчниками здорових кішок. Виявлено залежність застосування мегестролу ацетату із виникненням кістозних утворень в яєчниках із збільшенням яєчників у кішок дослідної групи у 1,7×2,47 рази при фолікулярній кісті та у 1,9×3,1 та 2,5×3,9 рази при лютеїновій кісті та полікістозі, відповідно. Встановлено збільшення матки за піометри у кішок при застосуванні мегестролу ацетату в 3,16×1,93 рази правого рогу і 2,84×2,1 рази лівого рогу порівняно із маткою здорових кішок. З'ясовано динаміку прогестерону (підвищення на 1,83%), фолікулостимулюючого гормону (зниження на 43,75%) та естрадіолу (підвищення на 72,15%) порівняно із інтактними тваринами. Обґрунтовано підвищення рівня глюкози у сироватці крові у кішок після застосування мегестролу на 34,31%, загального білку на 25,0% та креатиніну на 11,10%, аспартатамінотрансферази на 43,84% (1,78 рази) та алатамінотрансферази на 49,84% (1,99 рази), сечовини сироватки крові на 58,71%. При цьому же час зниження рівня гемоглобіну на 16,5%. Результати досліджень можуть бути використані при розробці нових методів та схем медикаментозної контрацепції з мінімізацією ризиків щодо ускладнень з боку репродуктивної системи, регулювання репродуктивної здатності та профілактиці неплідності у кішок.

Ключові слова: контрацептиви; гестагени; мегестролу ацетат; кісти; піометра; ендометрит