SUMMARY

The PhD thesis entitled “**Research regarding ovarian and uterine diseases in bitch**” has been developed in the Doctoral School of the University of Agricultural Sciences and Veterinary Medicine "Ion Ionescu de la Brad" University.

The thesis contains 185 pages and consists of two main parts, according to the currently regulations. A total number of 303 bibliographic titles from the national and international literature were used as a source of documentation. The data presented in the second part of the thesis are supported by a total number of 75 figures and 17 tables.

The originality of the research results from using uterine biopsy samples for investigation of uterine histopathological lesions in some bitches with fertility issues, as well as highlighting the histopathological details encountered in the case of various ovarian disorders in the bitch, especially in the context of the coexistence of uterine pathologies. Also, the results of the application of certain drug therapies in the treatment of the pyometra are reported for the first time in Romania, as an alternative to classic, surgical treatment, respectively the use of two different protocols, represented by aglepristone-cloprostenol and cabergoline-cloprostenol for the treatment of both the closed and opened-cervix pyometra. Also, for the first time in Romania, the thesis presents the use of laparoscopic surgical technique in veterinary medicine in treating ovarian disorders in the bitch as an alternative to the classic surgical treatment.

The first part, entitled "The Current Status of Knowledge", comprises three chapters (29 pages), provides information available in the literature on the morphology and physiology of the reproductive tract in the bitch, on the physiology of the reproductive function in the bitch, as well as information on ovarian pathology in the bitch, including details about the ovarian cysts, the remnant ovarian syndrome and ovarian neoplasia. Part I also includes bibliographic data on uterine pathology in the bitch, including aspects of metritis, placental sites sub involution, pyometra and cystic endometrial hyperplasia, as well as data on uterine neoplasia in this species.

The second part, entitled “PERSONAL CONTRIBUTIONS”, contains a total of 127 pages and it is divided into 7 chapters, presenting the aims and importance of the research, the materials and methods used, the results obtained, as well as the interpretation of the results, discussions and conclusions based on them.

The thesis contains original data that was published in scientific papers supported by symposiums organized by the Faculty of Veterinary Medicine Iasi or other faculties in the country, as well as other specialized magazines in the country.

The first chapter of the second part of the thesis (Chapter IV) presents the purpose and objectives of the research, namely:

- assessing the incidence of reproductive system diseases in domestic carnivores in two different geographical areas;

- establishing the haematological and biochemical blood profile that is characteristic of the main uterine disorders in the bitch: pyometra and cystic endometrial hyperplasia (CEH);

- analysis of the main systemic effects that the pyometra exerts on the bitch;

- highlighting the characteristic echographic aspects of ovarian and uterine diseases in the bitch;

- testing a modern method commonly used in human medicine, but rarely in the veterinary field, namely laparoscopic ovariectomy as an alternative to classical ovariectomy;

- testing the efficacy of drug therapy in pyometra of the bitch, as an alternative to surgical treatment;

- establishing the association between ovarian and uterine subclinical disorders and infertility in the bitch;

- highlighting the histopathological aspects encountered in reproductive disorders in the bitch.

Chapter V, called "Research on the incidence of reproductive pathologies in the bitch", was designed to evaluate the main reproductive diseases with which domestic canines are diagnosed, also looking for an age and race morbidity assessment of the genital tract disease in the bitch. In order to achieve this objectives, data from the Register of Consultations and Treatments of two clinics attached to the Veterinary Reproduction Department of Romania and Germany were analyzed for a period of four years. The data analyzed included information on the total number of pets, patients in the clinic. Information on the main reproductive diseases diagnosed in clinics in patients represented by domestic canines were also analyzed. In particular, it was notet the incidence of pyometra, vaginitis, vulvo-vaginitis, vaginal prolapse, vestibular-vaginal tumors, cervicitis, endometritis, metrites, uterine neoplasms, ovarian cysts, ovarian neoplasms etc., as well as the incidence of obstetrical diseases and mammary disorders (including mastitis, mastosis, breast tumors, false lactation).

The results showed that out of the total number of patients enrolled during the 4 years under the study, in both clinics the largest number of patients was represented by dogs. Of these, a very large proportion in both clinics was represented by the bitches, so it can be concluded that females have far more genital tract pathologies and much more frequently than males. Among the gynecological conditions encountered in the bitch, in both clinics studied, a significant

proportion is occupied by the pyometra. However, a significant percentage of the total pathologies encountered in the bitch is represented by mammary diseases, namely mastitis, mastoses and neoplastic formations.

Chapter VI, entitled ”Research on Clinical and Laboratory Diagnosis of Uterine Disorders in Bitch”, is structured on two subchapters.

The first subchapter, called "Clinical and Laboratory Diagnostics of the Pyometra Compared to CEH", aimed to analyze the various haematological and blood biochemical parameters as well as some clinical aspects for bitches with pyometra and those diagnosed with non-inflammatory uterine disease (CEH. The final goal of this study was to highlight elements that differentiate CEH of pyometra, considering that the symptoms of these two pathological entities are often the same, but the therapeutic approach is different. For the patients under study, some anamnestic and clinical data were noted, as well as data on the following hematological and biochemical parameters such as: leukocytes, total neutrophils, segmented neutrophils, lymphocytes, monocytes, eosinophils, basophils, erythrocytes, reticulocytes, hematocrit, hemoglobin, MCV (mean blood volume)), platelets, albumin, ammonia, bile acids, conjugated bilirubin, cholesterol, creatinine, fibrinogen, globulins, total protein, urea, GLDH (glutamate dehydrogenase), ALAT (alanine aminotransferase), ALP(alkaline phosphatase). All data on the cases studied were included in a common data base and processed using IBM SPSS® Statistics version 21 (IBM® Corporation, Chicago, IL, USA).

The results have showed that although the two pathologies may have a similar clinical developement, making it difficult for the clinician to distinguish them, for the patients with pyometra the respiratory and cardiac frequencies were higher, patients diagnosed with this disease presenting in a greater number changes in the color of the mucous membranes. At the same time, symptoms such as abdominal distension, vomiting, diarrhea, polyuria-polydipsia, although present in the patients of both analyzed groups,they were more common in those affected by pyometra. Hematological and biochemical blood test revealed for the pyometra patients an inflammatory leucograme, with a left shift, a regenerative, normochromic, normocytic anemia, also elevated levels of bile acids, conjugated bilirubin, creatinine, globulins as well as an increased level of GLDH, but a lower ALT compared to patients affected by cystic endometrial hyperplasia.

In the subchapter titled "Analysis of systemic effects of pyometra in bitch" it was followed, on the one hand, the evaluation of the differences on the basis of symptoms and blood biochemical parameters between the two forms of evolution of pyometra and, on the other hand, the evaluation of the percentage of dogs with pyometra presenting SIRS (Systemic Inflammatory

Response Syndrome). For these, two groups of bitches with opened-cervix pyometra and, respectively closed-cervix pyometra were analyzed as regards simptomatology and some biochemical blood parameters, any differences between the two subgroups were evidenced by the Independent t-test statistical analysis. The study revealed that patients diagnosed with opened- cervix pyometra showed a trend towards hyperthermia and bradycardia, while patients diagnosed with a pyometra evolving with a closed cervix showed more frequent hypothermia, tachycardia and anorexia or low appetite. Regarding the blood biochemical parameters, in both types of pyometra it was found a normochromic, normocytic anemia, but in the case of closed cervix pyometra it was more marked; also a more pronounced leukocytosis was noted in bitches affected by closed cervix pyometra. Higher values of bilirubin, cholesterol, creatinine, GLDH and ALP were noted for bitches without vaginal discharge. On the other hand, statistically significantly higher values were obtained for patients with vulvar discharge in terms of mean serum albumin and ALAT. Approximately one third of the total number of bitches with pyometra (32%) presented at least two of the signs indicated in the literature as being specific to the Systemic Inflammatory Response Syndrome (SIRS).

In Chapter VII, " Research on the imaging diagnosis of utero-ovarian disorders in the bitch", the aim was to highlight the characteristic echographic aspects in ovarian and uterine diseases in the bitch. The study highlights the usefulness of the ultrasound exam in diagnosing ovarian and uterine disorders in the bitch and presents the details that can be observed in the ultrasonographic exam for ovarian cysts, ovarian and uterine neoplasia, sub-involution of the placental sites, pyometra, cystic endometrial hyperplasia, as well as rare diseases such as ovarian hematoma, hydro-ovaries or the ovarian cortex within the Remnant Ovarian Syndrome.

Chapter VIII, entitled " Research on histopathology of uterine and ovarian diseases in bitch", is structured on two subchapters.

In the subchapter "Determining the causes of infertility in the bitch by histopathological analysis of uterine biopsy samples", the aim of the study was to observe the eventual uterine histological changes that may prevent the gestation of the bitch. For this purpose, uterine biopsy samples were collected by laparotomy from female dogs with reproductive problems such as failure to get pregnant or repeated gestational loss. The histopathological examination revealed that most of the patients had uterine lesions of varying degrees, unidentifiable by simple ultrasound examination. Among the lesions encountered, the most important were cystic endometrial hyperplasia alone or in association with pyometra, endometritis, fibrosis accompanied by endometrial glandular degeneration, pseudoplacental endometrial hyperplasia. Other isolated lesions were mucometra and adenomyosis. The study concluded that infertility in

bitches may be associated with endometrial lesions that are not detectable by clinical or ultrasound examination, and biopsy followed by histopathological analysis may be useful in establishing a diagnosis.

In the second subchapter, called "Histopathological diagnosis of ovarian conditions in the bitch", the aim of the study was to observe the histopathological details encountered in various ovarian diseases in the bitch, especially in the context of the concomitant presence of uterine pathologies. This study verified the presence of ovarian abnormalities in female dogs, either patients diagnosed by ultrasound with ovarian disease or patients that were diagnosed clinically and paraclinically with uterine disorders, to check the presence of ovarian anomalies for these, but also patients who did not show any clinical manifestation of utero-ovarian disorders to identify possible asymptomatic ovarian lesions. Following this study, it has been observed that uterine disorders such as pyometra commonly coexist with various ovarian conditions, such as ovarian cysts or persistent corpus luteum. Also, certain conditions such as ovarian atrophy or ovarian cysts as well as cystic enometrial hyperplasia may be omitted in clinical and ultrasound examinations. For such cases, the histopathological examination is the most effective diagnostic method.

Chapter IX, " Research on the therapy of uterine and ovarian diseases in the bitch", contains three subchapters.

The subchapter titled "Ovariectomy using laparoscopic technique - alternative to classical ovariectomy as a treatment of ovariopathies in the bitch" presents the necessary steps to perform this surgical technique in the case of patients who have some ovarian conditions, as well as the advantages it brings to veterinary practice such as: performing very small surgical incisions, better internal visualization of structures in the abdominal cavity, a faster post-operative recovery of patients, a much lower risk of operative infection, less stress and post-operative pain, a shorter hospitalization duration and low convalescence. However, the laparoscopic technique of ovariectomy has a number of disadvantages, including the high cost of intervention, as well as the need for special equipment and trained personnel, the risk of spleen perforation, a longer time of intervention for the less experienced staff.

The following subchapters present the application of two drug protocols that can be applied as an alternative treatment in pyometra therapy in bitches for which ovariohysterectomy was not desired. Thus, in the second subchapter there is presented a treatment scheme using the combination aglepristone-cloprostenol, and in the third subchapter the treatment scheme presented includes the use of cabergoline and cloprostenol. The results showed that in the aglepristone-cloprostenol-based therapy, a high success rate was achieved for 94.59% of the

subjects analyzed, resulting in a total healing within 28 days. The role of cloprostenol was observed after the first administration, noting visible progress in the evacuation of the uterine content , as well as the decreasig in diameter of the uterus. As minor side effects, some patients experienced lethargy, loss of appetite, and vomiting, but none of these symptoms were noticed from the second week of treatment.

As regards the second therapeutic protocol, cabergoline-cloprostenol, it has been shown to be effective for closed-cervix pyometra cases, in 83.3% of the cases the cervix was opened on the 2nd day of treatment, with the presence of vulvar discharge being observed, and in terms of uterine diameter, a gradual decrease was noticed, starting with the 2nd day of treatment. In all cases of closed-cervix pyometra, total healing was achieved by day 7 of treatment. For cases of opened-cervix pyometra, a 61.5% rate of gradual healing was achieved by day 7 of treatment.

Although encouraging results have been obtained in the use of both therapeutic protocols, complete and irreversible healing of the pyometra in the bitch can not be guaranteed, nor can the restoration of fertility, further studies are required on larger batches, over longer periods after the application of the treatment.

Chapter X, entitled "GENERAL CONCLUSIONS", presents the most important conclusions that are highlighted by the analysis of the researches carried out, as well as a series of suggestions and recommendations for the specialists in the field of Theriogenology of domestic canines.