

# Lymphoma in Cats: Contemporary perspectives

Dmytro Bilyi\* and Oleksandr Suprunenko



## Abstract

The past decade has witnessed active research in the field of feline veterinary oncology, focused on a deeper understanding of risk factors, key pathogenic mechanisms, prognostic markers, refinement of surgical techniques, exploration of new therapeutic targets, and neoplasia prevention. Despite certain advancements, the issue of verifying and predicting the biological behaviour of individual tumours remains unresolved. Among them is lymphoma, which often presents a chronic course (without pathognomonic signs) and demonstrates significant variability in tissue involvement, explaining the considerable fluctuations in its recorded frequency, ranging from 3.6 to 22%. The range of anatomical forms also varies significantly, with alimentary (up to 40%) and multicentric (up to 30%) lymphomas most commonly diagnosed. The probability of verifying numerous histopathological types (T-cell lymphoma, B-cell lymphoma) and their subtypes correlates with the anatomical form of lymphoma. A concerning trend is the dynamic increase in the registration of new and rare forms of lymphoma (primary lymphoma of the adrenal glands, pericardium, ocular globe, etc.), indicating the

variability of pathogenetic mechanisms, likely due to enhanced genomic instability. In addition to well-established risk factors for lymphoma in cats, the adverse anthropogenic impact has become relevant. The initiation of lymphoma in cats due to tobacco smoke has been proven. The significance of age, breed, and gender predisposition as risk factors for lymphoma has been debated and largely depends on the region. The absence of vaccination against viral diseases in cats increases the risk of lymphoma. The most significant risk factors for the development of lymphoma in cats are leukosis and immunodeficiency agents, although their etiological role has significantly decreased in recent years. Current research demonstrates the active involvement of chromosomal aberrations and chronic inflammation in lymphoma development. Kidney transplantation and immunosuppressive therapy increase the likelihood of lymphoma development in cats almost sevenfold. A risk factor requiring further study is genetic heredity, currently identified in Siamese, British, and Oriental shorthair cats.

**Key words:** *Cats; Tumours; Lymphoma; Risk factors; Anatomical forms*

## Introduction

Cancer is the leading cause of morbidity and mortality in domestic cats (Ludwig et al., 2022). Lymphoma (lymphosarcoma or malignant lymphoma) is the most common haematopoietic neoplasm in cats, and cats have the highest incidence rate of

lymphoma among all species (Louwerens et al., 2005).

Lymphoma is a neoplasm of lymphoid tissue with localised or systemic clinical signs. Unlike in dogs, where lymphoma typically manifests as a multicentric

Dmytro BILYI\*, DVM, Professor, (Corresponding author, e-mail: dmdmbeliy@ukr.net), Oleksandr SUPRUNENKO, Postgraduate, Faculty of Veterinary Medicine, Dnipro State Agrarian and Economic University, Dnipro, Ukraine

form involving lymphoid organs, in cats, visceral (involving the spleen/liver/intestines), extranodal, or nodal forms are more commonly diagnosed, with clinical signs depending on the affected organ/tissue (Mason and Pittaway, 2022).

In lymphoma, neoplastic transformation occurs in lymphoid cells of the immune system, hence any tissue or organ may be affected (Wolfesberger et al., 2018).

The most common types of tumours in cats are lymphoma (22%), sarcoma (15%), mast cell tumour (9%), and squamous cell carcinoma (7%). Haematopoietic tumours were diagnosed in 31% of cases; with malignant tumours: epithelial (19%) and mesenchymal (16%); and benign tumours: epithelial (16%), mesenchymal (13%); and other (5% of cases) (Schmidt et al., 2010).

Currently, the World Health Organization (WHO) classification is a relevant verification of lymphoma, used in both human and veterinary medicine (Wolfesberger et al., 2018), but it requires refinement.

The significant variability and high aggressiveness of lymphoma contribute to the complexity of diagnosis, the debated pathogenesis, and the low treatment efficacy. Difficulties arise in differentiating B-lymphoblastic lymphoma (B-LBL) from Burkitt lymphoma, and intestinal T-cell lymphoma (ITCL) demonstrates substantial morphological variability. Moreover, multicentric mature small cell lymphomas and thymic T-cell lymphomas have been diagnosed, although these categories are not codified by the WHO classification (Vezzali et al., 2010).

The diverse variations in clinical signs and histopathological changes in cats with lymphoma are associated with numerous factors, including adverse environmental influences, viral agent impacts, expression of pro-inflammatory proteins, gene mutations, etc. (Vail, 2007).

Considering the multifactorial aetiology and nonspecific course of the disease in most cases, the diagnostic scheme should include a maximum range of investigations: clinical, visual, histopathological, cytological, immunocytochemistry, immunohistochemistry, immunophenotyping using flow cytometry, and polymerase chain reaction. The more methods employed simultaneously or sequentially, the more reliable the diagnosis and precise the prognosis (Mihoković Buhin et al., 2020).

Furthermore, a dilemma arises when a clinician encounters a patient with solitary lymphoma, regardless of whether it is nodal (*i.e.*, stage IA patient) or extranodal. Should this tumour (or lymph node) be treated the same as any other solitary malignant neoplasm (*i.e.*, by wide surgical excision)? (Couto, 2001).

It should be noted that unlike most neoplasms, the anatomical form and clinical stage of lymphoma in cats are not directly related to the duration of the first response or survival period (Milner et al., 2005).

Thus, lymphoma in cats is characterised by its multifactorial aetiology and multidirectional biological behaviour, necessitating an objective assessment of accumulated information to determine further research directions.

Based on the relevance of studying the aetiological and pathogenetic aspects of lymphoma in cats, the research objective was to evaluate the degree of understanding of lymphoma in cats based on the analysis of published data on prevalence, anatomomorphological features, and risk factors for the disease.

## Anatomical and morphological characteristics of feline lymphoma

Four forms of lymphoma are distinguished in cats based on their anatomical

characteristics: multicentric (with disseminated involvement of lymph nodes, liver, spleen, and bone marrow), mediastinal (lesions localised in the lymph nodes of the thoracic cavity and/or infiltration of the bone marrow), alimentary (infiltration of the gastrointestinal tract and/or metastasis to abdominal lymph nodes), and extranodal (involvement of any organ: kidneys, nervous system, eyes, skin, etc.) (Couto, 2001). Unlike distribution based on anatomical features, the frequency of different cytomorphological types does not significantly differ: immunoblastic (18%), centroblastic (16%), globular leukocytic (15%), lymphocytic and lymphoblastic (12%), pleomorphic medium- and large-cell (10%), anaplastic large-cell (7%) (Sato et al., 2014).

Lymphoma has numerous subtypes. According to Wolfesberger et al. (2017), the diagnostic frequency of lymphoma subtypes was: peripheral T-cell lymphoma (37%), diffuse large B-cell (23%), intestinal T-cell and T-cell-rich B-cell (10%), large granular lymphocytic and anaplastic large T-cell (7%), B-cell small lymphocytic and T-cell angiotropic lymphoma (3%).

According to retrospective and prospective studies by Silva et al. (2022), the most common anatomical forms of lymphoma in cats are gastrointestinal (40.3%), multicentric (29%), mediastinal (17.7%), and extranodal (12.9%); subtypes include diffuse large B-cell lymphoma (DLBCL) (30.6%), peripheral T-cell lymphoma (PTCL) (29%), and enteropathy-associated T-cell lymphoma (EITL) type 2 (14.5%).

Cristo et al. (2019) provide the following structure of lymphoma incidence in cats. By anatomical forms: multicentric (43.4%), mediastinal (33.96%), renal (11.32%), hepatic (5.66%), nodal (3.77%), alimentary (1.89%); by histopathological types: small cell (33.96%), mixed diffuse (22.64%), immunoblastic (15.11%),

lymphoblastic (11.32%), small cell (9.43%), large cell (3.77%). According to Leite-Filho et al. (2018), the frequency of lymphoma registration in cats was: 50% mixed, 25% mediastinal, 12.5% alimentary and atypical. The most common subtype was diffuse large B-cell lymphoma (56%).

Rogato et al. (2022) noted the highest prevalence of medium- and large-cell lymphomas: mediastinal (42%), disseminated (30%), renal (15%) against the background of detection of FeLV in only 10% of cats and 100% negative results of FIV research.

Alimentary lymphoma, the most common anatomical form of lymphoma in cats, encompasses a group of diseases focused on the gastrointestinal tract with variable extraintestinal involvement. Three histological grades of AL are distinguished: low (LGAL), intermediate (IGAL), and high (HGAL). Additionally, a separate histological subclassification of AL is described - large granular lymphocytic lymphoma (LGLL), which can be of any grade (Barrs and Beatty, 2012). In 9.9% of patients, large-cell lymphoma was concurrently verified with small-cell lymphoma, characterised by changes in haematocrit, albumin, and total protein (Wright et al., 2019).

Leite-Filho et al. (2020) demonstrated a significant prevalence of alimentary (42/125) and mediastinal (35/125) lymphoma in cats against a background of positive retroviral immunostaining in 79 of 125 samples, indicating their important aetiological role. The average age of cats with T-cell lymphoma (66/125) was 120 months (10-240 months), while for B-cell lymphoma (59/125) it was 60 months (6-204 months). The most common alimentary tumour was T-cell lymphoma (type 1), associated with enteropathy, while mediastinal tumours were diffuse large B-cell lymphoma.

According to Pohlman et al. (2009), the proportion of gastrointestinal lymphomas accounted for 24%, with 18% localised solely in the stomach (all of B-cell origin), 78% affecting the small intestine (52% B-cell, 38% T-cell), and 16% affecting the large intestine (88% B-cell, 12% T-cell).

B-cell lymphomas (more often diffuse large-cell centroblastic type) manifested as transmural lesions of the stomach, small intestine, and ileocecal-colonic junction. T-cell lymphomas, characterised by specific mucosal architecture, CD3 expression, and clonal expansion, predominated in the gastrointestinal tract of cats (Moore et al., 2012).

Chronic enteric diseases, accompanied by signs of small intestinal thickening, exhibit histological features of lymphoma in approximately half of cases (Norsworthy et al., 2015).

Verified B-cell (more often) and T-cell (less frequently) intra- and periocular lymphomas represent metastatic lesions in cases of multicentric presentation (Ota-Kuroki et al., 2014; Bandinelli et al., 2020). The most prevalent subtype was diffuse large B-cell lymphoma (53%) and peripheral T-cell lymphoma (27%). Other subtypes included anaplastic large T- (5%) and B-cell (2.5%) lymphomas, while 15 cases (9%) were negative for all immunohistochemical markers (Musciano et al., 2020).

Described is lymphoma (lymphosarcoma) affecting the nervous system, characterised by a wide spectrum of morphological changes, including intraparenchymal brain formation, brain lymphomatosis, intravascular lymphoma, choroiditis lymphomatosis, and meningitis, extradural, intradural-extramedullary, or intramedullary spinal lymphoma, or neurolymphomatosis of the peripheral nerves. It more commonly develops in the spinal cord in the context of multicentric disease pro-

gression but may also manifest as a paraneoplastic process accompanying peripheral neuropathies (Mandara et al., 2016).

Mello et al. (2019) observed nervous system involvement in 12.8% of cats with lymphoma. In the majority of cases, they were represented by FeLV-positive secondary spinal cord B-cell lymphomas with an average age of 24 months.

Primary cerebellar B-cell lymphoma has been described in cats, demonstrating tumour cells resembling Hodgkin lymphoma, with FeLV protein expression (Yoshino et al., 2017).

Upper respiratory tract (URT) lymphomas are characterised as highly aggressive with predominantly primary nasal B-cell origin. Although primary nasal and nasopharyngeal lymphomas are considered distinct pathological entities, no differences in their clinical behaviour have been established. URT lymphomas may be initiated by lymphoplasmacytic inflammation and FeLV infection (Santagostino et al., 2018).

Cutaneous lymphomas at injection sites (CLIS) exhibit common clinical and pathological features with sarcomas at injection sites in cats and lymphomas developing against a background of subacute or chronic inflammation, similar to humans. Persistent inflammation caused by injection and reactivation of FeLV expression may contribute to the development of CLIS (Roccabianca et al., 2016).

Subcutaneous lymphoma in cats may mimic sarcoma, with high local (43.5%) and distant (32.2%) recurrence potential and a mean overall survival of 148 days (Meichner and Von Bomhard, 2016).

A widely observed phenomenon is the formation of lymphoma with sarcoma-like features against a background of subacute or chronic inflammation at injection sites. Persistent inflammation caused by injection and FeLV expression reactiva-

tion are considered risk factors for cutaneous lymphoma (CLIS), which is verified as primary angiocentric, angioinvasive predominantly large-cell lymphoma with aggressive clinical behaviour (Roccabianca et al., 2016).

Bilateral kidney involvement with possible metastatic liver and lung involvement is typically observed in cats. According to statistics, extranodal lymphoma, particularly the renal form, accounts for 7-30% of cases, mostly in cats over five years old. It is characterised by a significant risk of metastasis to the lungs and liver, as well as enhanced expression of diffuse B-cell lymphoma markers - CD79a (B-cell antigen receptor complex-associated protein alpha chain) and Ki-67 (marker of proliferation) (Oriekhova and Shchebentovska, 2023).

According to Williams et al. (2021), in the disease prevalence structure, the renal form comprises 3.6%, with half of cases being a component of multicentric lymphoma with a small percentage of stages IV and V.

Little et al. (2007) identified only diffuse lymphoid neoplasms, which in 91% of cases were classified as immunoblastic lymphomas. Nasal lymphoma was diagnosed more frequently than nasopharyngeal lymphoma in cats. In both cases, they were typically represented by B-cell immunoblastic tumours, positive for CD79a (B-cell antigen receptor complex-associated protein alpha chain).

Animals with intraocular or conjunctival lymphoma accounted for 0.1% and 0.08% of patients with lymphoma, respectively. Cats with intraocular lymphoma comprised 0.19% of all patients with uveitis, while conjunctival lymphoma occurred in 0.16% of all patients with conjunctivitis. Tumours included B-cell, non-B-cell, non-T-cell, and T-cell neoplasms. Metastases to lymph nodes were detected

in two cases of conjunctival lymphoma in cats (Wiggans et al., 2014).

Demonstrated was the absence of a clear distinction between leukaemia (LGL) and lymphoma in cats; both diseases originate from T-cytotoxic (CD3+/CD8+) or NK lymphocytes, have similar courses, and are characterised by aggressive behaviour (Valli et al., 2016).

A rare subtype, large granular lymphocyte (LGL) lymphoma, at the time of detection, is characterised by circulating neoplastic cells, a high level of serum lactate dehydrogenase (LDH), and a lack of response to drug therapy (Finotello et al., 2018).

A case of confirmed primary B-cell lymphoma of the adrenal glands in a cat was described, accompanied by hypoadosteronism (Romine et al., 2016).

A rare extranodal manifestation of lymphoma is described - primary laryngeal/tracheal lymphoma in cats (PLTL), which mostly exhibited a B-cell phenotype of low to intermediate differentiation (Rodriguez-Piza et al., 2023).

One of the rare forms in cats is primary pericardial lymphoma, represented by both T and B-cell immunophenotypes (registered with approximately equal frequency) (Amati et al., 2014).

A report on a rare form of cutaneous lymphoma was published - primary multifocal non-epitheliotropic B-cell lymphoma, presenting as individual dermal and subcutaneous formations of various sizes in the paw region (Quintavalla et al., 2020).

Published data on feline lymphoma are diverse and, in many cases, lack an analysis of the obtained results, complicating the determination of clinical and biological regularities in the course of the disease. Summarising the information provided, attention should be focused on the necessity of a unified methodological approach to verifying feline lymphoma



and creating a single database of oncological animals.

## Risk factors for lymphoma in cats

The high prevalence of malignant neoplasms in cats, including lymphomas, is associated with adverse anthropogenic influence due to changes in the environment and loss of genetic diversity (Vascellari et al., 2009). Lymphomas may exhibit age, breed, and gender predispositions depending on the region. Gabor et al. (1998) demonstrated that, unlike in other countries, males in the older age group predominated among patients ( $P=0.05$ ); the most common occurrences were kidney involvement, mixed, and atypical forms, with mediastinal form being more frequently diagnosed in young cats.

According to Economu et al. (2021), male cats older than 5 years have an increased risk of developing lymphoma (OR: 1.7, 95% CI: 1.2-2.4), and vaccinated animals have lower chances compared to non-vaccinated ones (OR: 0.7, 95% CI: 0.5-1.0). However, no correlation was established between the incidence of lymphoma and breed or environmental factors.

A retrospective assessment of lymphoma cases during the period 1985–2015 conducted by Kutlu et al. (2018) indicated a verification frequency of 2.54% in cats, with an average age of affected animals of 9 years, without significant gender or breed predispositions.

Results regarding the increased risk of malignant lymphoma in cats due to passive smoking have been published. A linear trend of increased risk associated with the duration and quantity of exposure was presented: animals exposed to environmental tobacco smoke (ETS) for more than 5 years had a relative risk of 3.2 (95% CI 1.5-6.9,  $P=0.003$ ) compared to cats

in households without smoking (Bertone et al., 2002).

Smith et al. (2020) did not find a significant correlation between ETS biomarkers and gastrointestinal lymphoma in cats; however, a connection may exist, requiring further investigation. Nicotine concentration in cat fur can be used as a biomarker of tobacco smoke exposure, allowing future studies to assess whether cats are at an increased risk of certain diseases.

In recent years, research on viral mechanisms underlying tumour transformation in the development and progression of cancer has been at the forefront, in both human and veterinary oncology. Oncogenic viruses in veterinary medicine play a crucial role, not only as causative agents in domestic animals, but also as models of malignant neoplasms, aiding in understanding the mechanisms of disease in both animals and humans (Parisi et al., 2023).

Research has shown that some infectious agents may play a direct role in neoplasia development, while others may induce neoplasia through changes in the immune response or by creating a pro-inflammatory environment. Feline leukaemia virus was one of the first infectious agents recognised as an oncogenic organism to attract significant attention. Subsequently, the oncogenic role of viruses in cats, including gammaherpesviruses, murine mammary tumour virus, papillomaviruses, hepadnaviruses, as well as *Helicobacter* and parasitic agents such as *Platynosomum fastosum* and *Opisthorchis viverrini*, has been established (Rolph and Cavanaugh, 2022).

The most widely recognised causes of lymphoma in cats are the gammaretroviral feline leukaemia virus (FeLV) and the lentiviral feline immunodeficiency virus (FIV). Currently, the mechanisms of oncogenic transformation caused by them

remain incompletely understood (Beatty, 2014).

Feline leukaemia virus (FeLV) is a risk factor for the development of mediastinal lymphoma, which is frequently detected in FeLV-positive animals (de Azevedo et al., 2022).

Recently, domestic cat hepadnavirus (DCH), similar to human hepatitis B virus (HBV), was detected in serum and liver samples from domestic cats with chronic hepatitis and hepatocellular carcinoma. Molecular studies conducted by independent research groups worldwide have shown positivity rates ranging from 6.5–12.5% in blood samples and up to 14.0% in liver tissue (Fruci et al., 2022). Currently, its role as a risk factor for lymphoma in cats is being investigated. DCH DNA was detected in 16.18% of blood samples ( $P=0.002$ ; OR: 5.15; 95% CI: 2.33–11.36) and 9.52% of tumour samples obtained from cats with lymphoma, compared to only 3.61% of blood samples from cats without lymphoma. In DCH-positive lymphoma, 50% of cats simultaneously had feline leukaemia virus, and in 100% of cases, it was associated with B-cell ( $P>0.9$ ; OR: 1.93; 95% CI: 0.09–37.89) and multicentric forms of lymphoma ( $P=0.008$ ; OR: 1.327; 95% CI: 0.06–31.18) (Beatty et al., 2023; Piewbang et al., 2023).

Recent data indicate a significant decrease in the role of viral agents (such as feline leukaemia virus (FeLV) and feline immunodeficiency virus (FIV)) in lymphoma development, leading to changes in the occurrence of specific anatomical subtypes and worsening treatment outcomes. Whereas in the past, young Siamese cats were more commonly affected, predominantly with mediastinal lymphomas, today the most common forms of lymphoma are nasopharyngeal and alimentary forms in older cats. However, these changes cannot be explained solely

by the prevalence of FeLV/FIV (Versteegh et al., 2023).

The age susceptibility of cats to lymphoma is bimodal: the first peak is observed in 2-year-old FeLV-positive cats, while the second peak occurs in 10–12-year-old predominantly FeLV-negative animals. The average age of cats with lymphoma is: 3 years for FeLV-positive cats and 7–8 years for FeLV-negative cats.

While in the past, lymphoma development was typically associated with FeLV and FIV, genomic abnormalities are now considered the direct cause. Increased expression of MDR1 and COX-2, along with decreased CDKN1B expression, has been observed in these patients. Many studies have noted the interaction of p53-MDM2 proteins, which may induce chromosomal instability (Lin et al., 2021).

Current research has focused on studying the role of chromosomal aberrations in lymphoma development. Predicted associations have been reported between the amplification of feline DNA satellite sequences and the onset of genomic instability in lymphoma and fibrosarcomas, likely due to disturbances in centromere activity and the formation of aberrant marker chromosomes (Santos et al., 2006).

Francis et al. (1980) consider immunopositivity for the virus, combined with low levels of antibodies to the cell membrane antigen associated with feline oncornavirus (FOCMA), as the main risk factors for lymphoma.

Cats with low-grade alimentary lymphoma (LGAL) showed increased expression of MDR1 (multidrug resistance) and COX<sub>2</sub> (cyclooxygenase-2) genes compared to inflammatory bowel disease (IBD), indicating their role in LGAL pathogenesis (Castro-López et al., 2018).

Cats with gastrointestinal lymphoma demonstrated significantly higher expression of the apoptotic marker Bcl-2 (OR:

90; 95% CI: 5-95) compared to chronic enteritis, which serves as a disease predictor (Swanson et al., 2012).

The development and progression of small cell lymphoma can be initiated by local microbially mediated inflammation, resulting from changes in gut microbiota composition with an increased proportion of *Fusobacterium* spp. ( $P=0.046$ ) and *Bacteroides* spp. ( $P=0.036$ ) (Garraway et al., 2018).

Non-neoplastic T-cell lymphoproliferative disease (LPD) has been described in British Shorthair kittens, similar to autoimmune lymphoproliferative syndrome in humans (ALPS) (Aberdein, 2013). Its probable hereditary nature is confirmed by defective T-cell apoptosis associated with a genetic defect in the FAS-mediated pathway (Aberdein et al., 2017).

High frequency of mediastinal lymphoma registration in young Siamese cats, with a significant predominance of males, suggests an important role of genetic factors in the etiopathogenesis of the disease (Fabrizio et al., 2014).

Significant correlations ( $P \leq 0.05$ ) were found between the histological structure and tumour localisation; age and localisation; leukaemia status; mitotic frequency; volume of necrosis and sclerosis. Significant correlations between the histopathological diagnosis and tumour topography included a higher number of cases of acute and chronic lymphoid leukaemia and multicentric tumour distribution (Valli et al., 2000).

Breed predisposition to lymphoma with a recessive type of inheritance has been described in Siamese and Oriental Shorthair cats (Louwerens et al., 2005).

The correlation between the localisation, histological structure, and immunophenotype of gastrointestinal lymphoma has been established, with a predominant gastric involvement of diffuse large B-cell lymphoma of the

immunoblastic nuclear type. However, the aetiological and pathogenetic significance of such a correlation, and the role of infectious agents (*Helicobacter* spp.) and resident lymphoid formations in disease initiation and progression, has not been determined (Pohlman et al., 2009).

Against the background of the development of modern treatment methods for chronic kidney diseases, cats have been shown to have a predisposition to the development of malignant neoplasia after kidney transplantation and immunosuppressive therapy (Wooldridge et al., 2002). Cats after transplantation had a 6.6-fold increased risk of developing malignant neoplasia and a 6.7-fold increased risk of lymphoma development. Therefore, owners should be informed about the need for lifelong monitoring (Wormser et al., 2016).

Based on the study results of renal lymphoma in cats (disease frequency of 3.6%), which in half of the cases was a component of multicentric lymphoma, Williams et al. (2021) concluded the lack of prognostic significance of the clinical stage or other factors and the necessity of further prospective studies.

Thus, risk factors for the development of lymphoma in cats may include external and internal factors. Published data in most cases are descriptive, not systematic, based on a small number of animals, reducing the reliability of statistical analysis and justifying the need for further study of possible disease causes.

## Conclusions

In the structure of neoplasms in cats, the proportion of lymphoma ranged from 3.6 to 22%, demonstrating significant clinical and morphological variability, which in addition to the chronic course and the absence of pathognomonic signs, complicates its detection. Among the anatomical



forms of feline lymphoma, gastrointestinal (up to 40%) and multicentric (up to 30%) forms are most commonly diagnosed. The frequency of verification of histological types (T-lymphoma and/or B-lymphoma) correlates with the anatomical forms of lymphoma. Over the past decade, there has been a trend towards an annual increase in the detection of rare and new forms/types of lymphoma. Among the risk factors, the most significant are anthropogenic factors, vaccination status, viral disease agents – leukaemia and immunodeficiency, kidney transplantation, chronic inflammation, and genomic mutations. The roles of age, breed, gender, and heredity remained unclear in the initiation of feline lymphoma. Further research into direct and indirect factors that initiate oncogenesis in feline lymphoma is needed based on a standardised methodological approach.

## References

1. ABERDEIN, D. (2013): Investigations of a novel lymphoproliferative disease in British shorthair kittens: a thesis presented in partial fulfilment of the requirements for the degree of Doctor of Philosophy at Massey University, Palmerston North, New Zealand (Doctoral dissertation, Massey University).
2. ABERDEIN, D., J. S. MUNDAY, B. GANDOLFI, K. E. DITTMER, R. MALIK, D. J. GARRICK and L. A. LYONS (2017): A FAS-ligand variant associated with autoimmune lymphoproliferative syndrome in cats. *Mamm. Genome* 28, 47-55. 10.1007/s00335-016-9668-1
3. AMATI, M., L. VENCO, P. ROCCABIANCA, S. F. SANTAGOSTINO and W. BERTAZZOLO (2014): Pericardial lymphoma in seven cats. *J. Feline Med. Surg.* 16, 507-512. 10.1177/1098612X13506199
4. BANDINELLI, M. B., M. VIEZZER BIANCHI, J. G. WRONSKI, L. SANTOS DE MELLO, R. BLANCO DEMARTINI, C. SAVI and S. PETINATTI PAVARINI (2020): Ophthalmopathologic characterization of multicentric or metastatic neoplasms with an extraocular origin in dogs and cats. *Vet. Ophthalmol.* 23, 814-827. 10.1111/vop.12803
5. BARRS, V. and J. BEATTY (2012): Feline alimentary lymphoma: 1. Classification, risk factors, clinical signs and non-invasive diagnostics. *J. Feline Med. Surg.* 14, 182-190. 10.1177/1098612X12439265
6. BEATTY, J. (2014): Viral causes of feline lymphoma: retroviruses and beyond. *Vet. J. (London, England: 1997)*, 201, 174-180. 10.1016/j.tvjl.2014.05.026
7. BEATTY, J. A., T. TU, P. A. PESAVENTO, J. P. CAVASIN, M. C. CHEN, J. A. LIDBURY, J. M. STEINER, V. R. BARRS, and J. M. CULLEN (2023): Domestic Cat Hepadnavirus and Lymphoma. *Viruses* 15, 2294. 10.3390/v15122294
8. BERTONE, E. R., L. A. SNYDER and A. S. MOORE (2002): Environmental tobacco smoke and risk of malignant lymphoma in pet cats. *Am. J. Epidemiol.* 156, 268-273. 10.1093/aje/kwf044
9. CASTRO-LÓPEZ, J., M. TELES, C. FIERRO, K. ALLENSPACH, M. PLANELLAS and J. PASTOR (2018): Pilot study: duodenal MDRI and COX2 gene expression in cats with inflammatory bowel disease and low-grade alimentary lymphoma. *J. Feline Med. Surg.* 20, 759-766. 10.1177/1098612X17730708
10. COUTO, C. G. (2000): Advances in the treatment of the cat with lymphoma in practice. *J. Feline Med. Surg.* 2, 95-100. 10.1053/jfms.2000.0079
11. CRISTO, T. G., G. BIEZUS, L. F. NORONHA, L. H. S. PEREIRA, J. A. WITHOEFT, L. V. FURLAN and R. A. CASAGRANDE (2019): Feline lymphoma and a high correlation with feline leukaemia virus infection in Brazil. *J. Comp. Pathol.* 166, 20-28. 10.1016/j.jcpa.2018.10.171
12. DE AZEVEDO, L. B., B. B. FENNER, S. DALEGRAVE, C. F. VEDANA, L. TOIGO, T. ÂNGELA, N. G. GAUER and E. C. DE OLIVEIRA (2022): Mediastinal Lymphoma in a Cat with Feline Leukemia Virus Mediastinal Lymphoma in a Cat with Feline Leukemia Virus. *Acta Sci. Vet.* 50. 10.22456/1679-9216.119979
13. ECONOMU, L., A. STELL, D. G. O'NEILL, I. SCHOFIELD, K. STEVENS and D. BRODBELT (2021): Incidence and risk factors for feline lymphoma in UK primary-care practice. *J. Small Anim. Pract.* 62, 97-106. 10.1111/jsap.13266
14. FABRIZIO, F., A. E. CALAM, J. M. DOBSON, S. A. MIDDLETON, S. MURPHY, S. S. TAYLOR and A. J. STELL (2014): Feline mediastinal lymphoma: a retrospective study of signalment, retroviral status, response to chemotherapy and prognostic indicators. *J. Feline Med. Surg.* 16, 637-644. 10.1177/1098612X13516621
15. FINOTELLO, R., M. E. VASCONI, S. SABATTINI, C. AGNOLI, C. GIACOBONI, M. ANNONI and L. MARCONATO (2018): Feline large granular lymphocyte lymphoma: An Italian Society of Veterinary Oncology (SIONCOV) retrospective study. *Vet. Comp. Oncol.* 16, 159-166. 10.1111/vco.12325
16. FRANCIS, D. P., M. ESSEX, R. M. JAKOWSKI, S. M. COTTER, T. J. LERER and J. R. W. D. HARDY (1980): Increased risk for lymphoma and glomerulonephritis in a closed population of cats exposed to feline leukemia virus. *Am. J. Epidemiol.* 111, 337-346. 10.1093/oxfordjournals.aje.a112905

17. FRUCI, P., F. DI PROFIO, A. PALOMBIERI, I. MASSIRIO, G. LANAVE, G. DIAKOUDI, F. PELLEGRINI, F. MARSILIO, V. MARTELLA and B. DI MARTINO (2022): Detection of antibodies against domestic cat hepadnavirus using baculovirus-expressed core protein. *Transbound Emerg. Dis.* 69, 2980-2986. 10.1111/tbed.14461
18. GABOR, L. J., R. MALIK and P. J. CANFIELD (1998): Clinical and anatomical features of lymphosarcoma in 118 cats. *Aust. Vet. J.* 76, 725-732. 10.1111/j.1751-0813.1998.tb12300.x
19. GARRAWAY, K., C. M. JOHANNES, A. BRYAN, J. PEAUROI, G. ROSSI, M. ZHANG and A. E. JERGENS (2018): Relationship of the mucosal microbiota to gastrointestinal inflammation and small cell intestinal lymphoma in cats. *J. Vet. Intern. Med.* 32, 1692-1702. 10.1111/jvim.15291
20. KUTLU, T., K. FILIKCI, M. Y. ABOU and O. KUTSAL (2018): A retrospective survey on canine and feline lymphomas (1985-2015). *Ankara Üniversitesi Veteriner Fakültesi Dergisi* 65, 93-98. 10.1501/Vetfak\_0000002833
21. LEITE-FILHO, R. V., W. PANZIERA, M. B. BANDINELLI and S. P. PAVARINI (2018): Pathological characterization of lymphoma with pulmonary involvement in cats. *J. Comp. Pathol.* 165, 6-12. 10.1016/j.jcpa.2018.09.007
22. LEITE-FILHO, R. V., W. PANZIERA, M. B. BANDINELLI, L. C. HENKER, K. DA CONCEIÇÃO MONTEIRO, L. G. CORBELLINI and S. P. PAVARINI (2020): Epidemiological, pathological and immunohistochemical aspects of 125 cases of feline lymphoma in Southern Brazil. *Vet. Comp. Oncol.* 18, 224-230. 10.1111/vco.12535
23. LIN, J., V. KOUZNETSOVA and I. TSIGELNY (2021): Molecular mechanisms of feline cancers. *OBM Genetics* 5, 1-29. 10.21926/obm.genet.2102131
24. LITTLE, L., R. PATEL and M. GOLDSCHMIDT (2007): Nasal and nasopharyngeal lymphoma in cats: 50 cases (1989-2005). *Vet. Pathol.* 44, 885-892. 10.1354/vp.44-6-885
25. LOUWERENS, M., C. A. LONDON, N. C. PEDERSEN and L. A. LYONS (2005): Feline lymphoma in the post-feline leukemia virus era. *J. Vet. Intern. Med.* 19, 329-335. 10.1892/0891-6640(2005)19[329:flitp]2.0.co;2
26. LUDWIG, L., M. DOBROMYLSKYJ, G. A. WOOD and L. VAN DER WEYDEN (2022): Feline Oncogenomics: What Do We Know about the Genetics of Cancer in Domestic Cats? *Vet. Sci.* 9, 547. 10.3390/vetsci9100547
27. MANDARA, M. T., L. MOTTA and P. CALÒ (2016): Distribution of feline lymphoma in the central and peripheral nervous systems. *Vet. J.* 216, 109-116. 10.1016/j.tvjl.2016.07.013
28. MASON, S. and C. PITTAWAY (2022): Feline lymphoma: diagnosis, staging and clinical presentations. In *Practice* 44, 4-20. 10.1002/inpr.163
29. MEICHNER, K. and W. VON BOMHARD (2016): Patient characteristics, histopathological findings and outcome in 97 cats with extranodal subcutaneous lymphoma (2007-2011). *Vet. Comp. Oncol.* 14, 8-20. 10.1111/vco.12081
30. MELLO, L. S., R. V. LEITE-FILHO, W. PANZIERA, M. B. BANDINELLI, L. SONNE, D. DRIEMEIER and S. P. PAVARINI (2019): Feline lymphoma in the nervous system: pathological, immunohistochemical, and etiological aspects in 16 cats. *Pesquisa Vet. Bras.* 39, 393-401. 10.1590/1678-5150-PVB-6295
31. MIHOKOVIĆ BUHIN, I., Š. NALETIĆ, M. PALIĆ and A. OGNJENOVIĆ (2020): Feline lymphoma. *Hrv. Vet. Vjesnik* 28, 70-74.
32. MILNER, R. J., J. PEYTON, K. COOKE, L. E. FOX, A. GALLAGHER, P. GORDON and J. HESTER (2005): Response rates and survival times for cats with lymphoma treated with the University of Wisconsin-Madison chemotherapy protocol: 38 cases (1996-2003). *J. Am. Vet. Med. Assoc.* 227, 1118-1122. 10.2460/javma.2005.227.1118
33. MOORE, P. F., A. RODRIGUEZ-BERTOS and P. H. KASS (2012): Feline gastrointestinal lymphoma: mucosal architecture, immunophenotype, and molecular clonality. *Vet. Pathol.* 49, 658-668. 10.1177/0300985811404712
34. MUSCIANO, A. R., M. R. LANZA, R. R. DUBIELZIG, L. B. TEIXEIRA and A. C. DURHAM (2020): Clinical and histopathological classification of feline intraocular lymphoma. *Vet. Ophthalmol.* 23, 77-89. 10.1111/vop.12692
35. NORSWORTHY, G. D., J. S. ESTEP, C. HOLLINGER, J. M. STEINER, J. O. LAVALLEE, L. N. GASSLER and M. KIUPEL (2015): Prevalence and underlying causes of histologic abnormalities in cats suspected to have chronic small bowel disease: 300 cases (2008-2013). *J. Am. Vet. Med. Assoc.* 247, 629-635. 10.2460/javma.247.6.629
36. ORIEKHOVA, K. and O. SHCHEBENTOVSKA (2023): Pathomorphology of the renal form of lymphoma in cats. *Regul. Mech. Biosyst.* 14, 3-9. 10.15421/022301
37. OTA-KUROKI, J., J. M. RAGSDALE, B. BAWA, N. WAKAMATSU and K. KUROKI (2014): Intraocular and periocular lymphoma in dogs and cats: a retrospective review of 21 cases (2001-2012). *Vet. Ophthalmol.* 17, 389-396. 10.1111/vop.12106
38. PARISI, F., N. FONTI, F. MILLANTA, G. FREER, M. PISTELLO and A. POLI (2023): Exploring the link between viruses and cancer in companion animals: a comprehensive and comparative analysis. *Infect. Agents Cancer* 18, 40. 10.1186/s13027-023-00518-7
39. PIEWBANG, C., S. W. WARDHANI, J. SIRIPOONSUB, S. SIRIVISOOT, A. RUNGSIPIPAT and S. TECHANGAMSUWAN (2023): Domestic cat hepadnavirus detection in blood and tissue samples of cats with lymphoma. *Vet. Q.* 43, 1-10. 10.1080/01652176.2023.2265172

40. POHLMAN, L. M., M. L. HIGGINBOTHAM, E. G. WELLES and C. M. JOHNSON (2009): Immunophenotypic and histologic classification of 50 cases of feline gastrointestinal lymphoma. *Vet. Pathol.* 46, 259-268.
41. QUINTAVALLA, F., R. DI LECCE, D. CARLINI, M. ZANFABRO and A. M. CANTONI (2020): Multifocal cutaneous non-epitheliotropic B-cell lymphoma in a cat. *J. Feline Med. Surg. Open Rep.* 6, 2055116920972077. 10.1177/2055116920972077
42. ROCCABIANCA, P., G. AVALONE, A. RODRIGUEZ, L. CRIPPA, E. LEPRI, C. GIUDICE and V. K. AFFOLTER (2016): Cutaneous lymphoma at injection sites: pathological, immunophenotypical, and molecular characterization in 17 cats. *Vet. Pathol.* 53, 823-832. 10.1177/0300985815623620
43. RODRIGUEZ-PIZA, I., J. F. BORREGO, E. TREGGIARI, S. VERGANTI, S. L. PRIESTNALL and A. LARA-GARCIA (2023): Clinical presentation, treatment and outcome in 23 cats with laryngeal or tracheal lymphoma. *J. Feline Med. Surg.* 25, 1098612X221143769. 10.1177/1098612X221143769
44. ROGATO, F., J. B. TANIS, B. PONS GIL, C. PITTAWAY, C. A. JOHNSTON and A. GUILLÉN (2023): Clinical characterisation and long-term survival of paediatric and juvenile lymphoma in cats: 33 cases (2008-2022). *J. Small Anim. Pract.* 64, 788-796. 10.1111/jsap.13667
45. ROLPH, K. E. and R. P. CAVANAUGH (2022): Infectious Causes of Neoplasia in the Domestic Cat. *Vet. Sci.* 9, 467. 10.3390/vetsci9090467
46. ROMINE, J. F., A. R. KOZICKI and M. S. ELIE (2016): Primary adrenal lymphoma causing hypoadosteronism in a cat. *J. Feline Med. Surg. Open Rep.* 2, 2055116916684409. 10.1177/2055116916684409
47. SANTAGOSTINO, S. F., C. M. MORTELLARO, P. BORACCHI, G. I. A. N. C. A. R. L. O. AVALONE, M. CANIATTI, A. FORLANI and P. ROCCABIANCA (2015): Feline upper respiratory tract lymphoma: site, cyto-histology, phenotype, FeLV expression, and prognosis. *Vet. Pathol.* 52, 250-259. 10.1177/0300985814537529
48. SANTOS, S., R. CHAVES, F. ADEGA, E. BASTOS and H. GUEDES-PINTO (2006): Amplification of the major satellite DNA family (FA-SAT) in a cat fibrosarcoma might be related to chromosomal instability. *J. Hered.* 97, 114-118. 10.1093/jhered/esj016
49. SATO, H., Y. FUJINO, J. CHINO, M. TAKAHASHI, K. FUKUSHIMA, Y. GOTO-KOSHINO and H. TSUJIMOTO (2014): Prognostic analyses on anatomical and morphological classification of feline lymphoma. *J. Vet. Med. Sci.* 76, 807-811. 10.1292/jvms.13-0260
50. SCHMIDT, J. M., S. M. NORTH, K. P. FREEMAN and F. RAMIRO-IBÁÑEZ (2010): Feline paediatric oncology: retrospective assessment of 233 tumours from cats up to one year (1993 to 2008). *J. Small Anim. Pract.* 51, 306-311. 10.1111/j.1748-5827.2010.00915.x
51. SILVA, D. H., R. ECCO, F. PIÉREZAN, G. D. CASSALI, J. K. REIS, A. B. GONÇALVES and F. O. LEME (2022): Classification of lymphoma in cats and its relationship with the detection of feline leukemia virus proviral DNA. *Pesqui Vet. Bras.* 42, e07021. 10.1590/1678-5150-PVB-7021
52. SMITH, V., C. KNOTTENBELT, D. WATSON, et al. (2020): Hair nicotine concentration of cats with gastrointestinal lymphoma and unaffected control cases. *Vet. Rec.* 186, 414. 10.1136/vr.105564
53. SMITH, V. A., A. R. MCBREARTY, D. G. WATSON, D. J. MELLOR, S. SPENCE and C. KNOTTENBELT (2017): Hair nicotine concentration measurement in cats and its relationship to owner-reported environmental tobacco smoke exposure. *J. Small Anim. Pract.* 58, 3-9. 10.1111/jsap.12616
54. SWANSON, C. M., R. C. SMEDLEY, P. V. SAAVEDRA, M. KIUPEL and B. E. KITCHELL (2012): Expression of the Bcl-2 apoptotic marker in cats diagnosed with inflammatory bowel disease and gastrointestinal lymphoma. *J. Feline Med. Surg.* 14, 741-745. 10.1177/1098612X12451404
55. VAIL, D. M. (2007): Hematopoietic tumors. In: Withrow, S. J., Vail, D. M. eds. *Small Animal Clinical Oncology*. 7<sup>th</sup> ed. Saint Louis: Elsevier Saunders; pp. 769-782.
56. VALLI, V. E., D. BIENZLE and D. J. MEUTEN (2016): Tumors of the hemolymphatic system. *Tumors in domestic animals*, 203-321. 10.1111/vco.12325
57. VALLI, V. E., R. M. JACOBS, A. NORRIS, C. G. COUTO, W. B. MORRISON, D. MCCAW, S. COTTER, G. OGILVIE and A. MOORE (2000): The histologic classification of 602 cases of feline lymphoproliferative disease using the National Cancer Institute working formulation. *Journal of veterinary diagnostic investigation: official publication of the American Association of Veterinary Laboratory Diagnosticians, Inc.* 12, 295-306. 10.1177/104063870001200401
58. VASCELLARI, M., E. BAIONI, G. RU, A. CARMINATO and F. MUTINELLI (2009): Animal tumour registry of two provinces in northern Italy: incidence of spontaneous tumours in dogs and cats. *BMC Vet. Res.* 5, 39. 10.1186/1746-6148-5-39
59. VERSTEEGH, H., M. M. ZANDVLIET, L. R. FEENSTRA, F. E. VAN DER STEEN and E. TESKE (2023): Feline Lymphoma: Patient Characteristics and Response Outcome of the COP-Protocol in Cats with Malignant Lymphoma in The Netherlands. *Animals* 13, 2667. 10.3390/ani13162667
60. VEZZALI, E., A. L. PARODI, P. S. MARCATO and G. BETTINI (2010): Histopathologic classification of 171 cases of canine and feline non-Hodgkin lymphoma according to the WHO. *Vet. Comp. Oncol.* 8, 38-49. 10.1111/j.1476-5829.2009.00201.x

61. WIGGANS, K. T., K. A. SKORUPSKI, C. M. REILLY, S. A. FRAZIER, R. R. DUBIELZIG and D. J. MAGGS (2014): Presumed solitary intraocular or conjunctival lymphoma in dogs and cats: 9 cases (1985–2013). *J. Am. Vet. Med. Assoc.* 244 460–470. 10.2460/javma.244.4.460
62. WILLIAMS, A. G., A. E. HOHENHAUS and K. E. LAMB (2021): Incidence and treatment of feline renal lymphoma: 27 cases. *J. Feline Med. Surg.* 23, 936–944. 10.1177/1098612X20984363
63. WOLFESBERGER, B., A. FUCHS-BAUMGARTINGER, V. GRESS, S. E. HAMMER, G. GRADNER, K. KNÖDL and C. BEHAM-SCHMID (2018): World Health Organization classification of lymphoid tumours in veterinary and human medicine: a comparative evaluation of gastrointestinal lymphomas in 61 cats. *J. Comp. Pathol.* 159, 1–10. 10.1016/j.jcpa.2017.12.006
64. WOLFESBERGER, B., O. SKOR, S. E. HAMMER, I. FLICKINGER, M. KLEITER, B. C. RÜTGEN and A. FUCHS-BAUMGARTINGER (2017): Does categorisation of lymphoma subtypes according to the World Health Organization classification predict clinical outcome in cats? *J. Feline Med. Surg.* 19, 897–906. 10.1177/1098612X16666119
65. WOOLDRIDGE, J. D., C. R. GREGORY, K. G. MATHEWS, L. R. ARONSON and A. E. KYLES (2002): The prevalence of malignant neoplasia in feline renal-transplant recipients. *Vet. Surg.* 31, 94–97. 10.1053/jvet.2002.30540
66. WORMSER, C., A. MARIANO, E. S. HOLMES, L. R. ARONSON and S. W. VOLK (2016): Post-transplant malignant neoplasia associated with cyclosporine-based immunotherapy: prevalence, risk factors and survival in feline renal transplant recipients. *Vet. Comp. Oncol.* 14, e126–e134. 10.1111/vco.12120
67. WRIGHT, K. Z., A. E. HOHENHAUS, A. M. VERRILLI and S. VAUGHAN-WASSER (2019): Feline large-cell lymphoma following previous treatment for small-cell gastrointestinal lymphoma: incidence, clinical signs, clinicopathologic data, treatment of a secondary malignancy, response and survival. *J. Feline Med. Surg.* 21, 353–362. 10.1177/1098612X18779870
68. YOSHINO, Y., J. K. CHAMBERS, T. NAKAMORI, Y. GOTO-KOSHINO, K. NISHIGAKI, H. TSUJIMOTO and K. UCHIDA (2017): Primary cerebellar lymphoma with Hodgkin lymphoma-like morphology in a cat. *J. Vet. Diagn. Invest.* 29, 707–710. 10.1177/1040638717704239

## Limfom u mačaka – suvremeni pogled na problematiku

Dmytro BILYI, DVM, Professor, Oleksandr SUPRUNENKO, Postgraduate, Faculty of Veterinary Medicine, Dnipro State Agrarian and Economic University, Dnipro, Ukraine

Prošlo desetljeće svjedočilo je aktivnom istraživanju na polju veterinarske onkologije mačaka, usredotočenom na duboko razumijevanje čimbenika rizika, ključnih patogenih mehanizama, prognostičkih markera, usavršavanje kirurških tehnika, istraživanje novih terapijskih ciljeva i prevencije neoplazija. Unatoč određenim napretcima, pitanje potvrđivanja i predviđanja biološkog ponašanja pojedinačnih tumora ostaje neriješeno. Među njima je i limfom, koji je često kroničnog tijeka (bez patognomskih znakova) i pokazuje znatnu varijabilnost uključenosti tkiva, što objašnjava značajna kolebanja u njegovoj učestalosti registracije – koja variraju od 3,6 do 22 %. Distribucija anatomskih oblika isto tako značajno varira, s tim da su alimentarni (do 40 %) i multicentrični (do 30 %) limfomi najčešće dijagnosticirani. Vjerojatnost potvrđivanja brojnih patohistoloških vrsta (T-stanični limfom, B-stanični limfom) i njihovih podtipova povezana je s anatomskim oblikom limfoma. Zabrinjavajući trend je dinamičko povećanje registracije novih i rijetkih oblika limfoma (primarni limfom nadbubrežnih žlijezda, perikardija, očne jabučice, itd.), ukazu-

jući na varijabilnost patogenetskih mehanizama, vjerojatno zbog povećane genomske nestabilnosti. Uz dobro utvrđene čimbenike rizika za limfom u mačaka, nepoželjni antropogeni učinak postao je relevantan. Početak limfoma u mačaka zbog duhanskog dima je dokazan. Raspravlja se o značenju predispozicije dobi, pasmine i spola kao čimbenika rizika za limfom i uvelike ovisi o regiji. Izostanak cijepjenja protiv virusnih bolesti u mačaka povećava rizik od limfoma. Najznačajniji čimbenici rizika za razvoj limfoma u mačaka su leukoza i agensi imunodeficiencije, premda se njihova etiološka uloga značajno smanjila posljednjih godina. Trenutna istraživanja pokazuju aktivnu uključenost kromosomskih aberacija i kromosomske upale u razvoju limfoma. Transplantacija bubrega i imunosupresivna terapija gotovo sedam puta povećavaju vjerojatnost razvoja limfoma u mačaka. Čimbenik rizika koji zahtjeva dodatno istraživanje jest genetičko nasljeđivanje, trenutno prepoznato u sijamskih, britanskih i orijentalnih kratkodlakih mačaka.

**Ključne riječi:** mačke, tumori, limfom, čimbenici rizika, anatomske oblike