

## NEOPLASIA IN FELIDS AT THE KNOXVILLE ZOOLOGICAL GARDENS, 1979–2003

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**Abstract:** A review of medical records and necropsy reports from 1979–2003 found 40 neoplasms in 26 zoo felids, including five lions (*Panthera leo*, two males and three females), three leopards (*Panthera pardus*, two males and one female), one jaguar (*Panthera onca*, female), 11 tigers (*Panthera tigris*, three males and eight females), two snow leopards (*Panthera uncia*, one male and one female), two cougars (*Felis concolor*, one male and one female), one bobcat (*Felis rufus*, male), and one cheetah (*Acinonyx jubatus*, female). Animals that had not reached 3 yr of age or had been housed in the collection less than 3 yrs were not included in the study. Neoplasia rate at necropsy was 51% (24/47), and overall incidence of felid neoplasia during the study period was 25% (26/103). Neoplasia was identified as the cause of death or reason for euthanasia in 28% (13/47) of those necropsied. Neoplasms were observed in the integumentary-mammary ( $n = 11$ ), endocrine ( $n = 10$ ), reproductive ( $n = 8$ ), hematopoietic-lymphoreticular ( $n = 5$ ), digestive ( $n = 3$ ), and hepatobiliary ( $n = 2$ ) systems. One neoplasm was unclassified by system. Multiple neoplasms were observed in 11 animals. Both benign and malignant neoplasms were observed in all systems except for the hematopoietic-lymphoreticular systems where all processes were malignant. Of the endocrine neoplasms, those involving the thyroid and parathyroid glands predominated ( $n = 8$ ) over other endocrine organs and included adenomas and carcinomas. In the integumentary system, 63% (7/11) of neoplasms involved the mammary gland, with mammary carcinoma representing 83% (6/7) of the neoplasms. The rates of neoplasia at this institution, during the given time period, appears to be greater than rates found in the one other published survey of captive felids.

**Key words:** Felid, neoplasia, *Panthera leo*, *Panthera pardus*, *Panthera onca*, *Panthera tigris*, *Panthera uncia*, *Felis concolor*, *Felis rufus*, *Acinonyx jubatus*.

### INTRODUCTION

A great diversity of neoplasms has been reported in captive wild felids, but most reports are of single cases of neoplasia.<sup>6,9,16</sup> There have been reviews of neoplasia in zoo collections, but specific discussion of felid neoplasia could not be found.<sup>8,12,15,19</sup> Only one previous study has reported rates of neoplasia specifically for felids, and these rates were based on total necropsy accessions.<sup>15</sup>

A retrospective study was conducted to determine types and rates of neoplasia in a collection of zoo felids over 24 yr. Additionally, ages at diagnosis and whether neoplasia caused death or resulted in euthanasia were documented.

### MATERIALS AND METHODS

Inventory records for all felids held at the Knoxville Zoological Gardens (Knoxville, Tennessee, USA) from 1 January 1979 to 31 December 2003

were reviewed. Records of animals that had not reached 3 yr of age were excluded on the basis that they represented a low risk of neoplasia due to young age. Animals housed in the collection less than 3 yr were considered transient within the population and their medical and necropsy records were not included in this study. No attempt was made to follow up on animals transferred from the collection.

The 103 felids that fit the selection criteria, including animals with and without neoplasia, were held at the zoo during the study period (Table 1). Of these animals, 47 died during the study period. Forty-four felids had been held at the zoo for at least 3 yrs prior to being transferred from the collection. Twelve animals over the age of 3 yrs and that had been in the collection for at least 3 yrs were alive on 31 December 2003.

Necropsy reports, biopsy reports, and medical records for animals fitting these criteria were reviewed. All biopsies and bodies of animals that died were submitted for full examination to the Pathology Service of The University of Tennessee's College of Veterinary Medicine, Knoxville, Tennessee, USA.

The species, sex, age at diagnosis, age at death, whether the neoplasm was the cause of death, reason for euthanasia, or if the animal died or was euthanized for other reasons, diagnosis by necropsy

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**Table 1.** Population and neoplasia rates for a retrospective study of felids at the Knoxville Zoo from 1979–2003.

Common name	Species	Total population		No. of felids with neoplasia		Species-specific rate of neoplasia (%)	Species-specific rate of neoplasia at necropsy (%)	% cause of death <sup>a</sup>
		Males	Females	Males	Females			
Lion	<i>Panthera leo</i>	13	14	2	3	19	36	21
Leopard	<i>Panthera pardus</i>	5	4	2	1	33	75	25
Jaguar	<i>Panthera onca</i>	3	3	0	1	17	33	33
Tiger	<i>Panthera tigris</i>	14	19	3	8	33	69	38
Snow leopard	<i>Panthera uncia</i>	2	2	1	1	50	100	50
Bobcat	<i>Felis rufus</i>	2	5	1	0	14	100	100
Cougar	<i>Felis concolor</i>	3	3	1	1	33	100	0
Cheetah	<i>Acinonyx jubatus</i>	4	5	0	1	11	33	0
Canadian lynx	<i>Felis canadensis</i>	1	1	0	0	0	0	0
				Overall neoplasia		Neoplasia necropsy		
				rate (%)		rate (%)		
Total		47	56	10	16	25	51	27.7

<sup>a</sup> Percentage of deaths or euthanasias that were caused by neoplasia.

or biopsy, type of neoplasia, number of neoplasms, evidence of metastasis, and metastatic sites were recorded for each animal. Implantation with melen-gestrol acetate (MGA) implants was recorded for lions and tigers, due to previous association of use of MGA with neoplasia.<sup>11,20</sup> The cause of death, or the reason for euthanasia, was based on interpretation of the medical and necropsy records.

Necropsy neoplasia rate (NNR) was determined by the number of animals with neoplasia found at necropsy divided by the number of felids that met the selection criteria and had been necropsied. The overall rate of neoplasia (ONR) was calculated by dividing the number of animals diagnosed with neoplasia, whether by biopsy or necropsy, by the total number of each felid that fit the selection criteria. The species-specific rate of neoplasia (SSR) was calculated similarly to ONR, but only using data on animals within a single species, and the species-specific necropsy rate (SSNR) was calculated similarly to NNR, but within an individual species. All rates were reported as percentages.

## RESULTS

A total of 40 separate neoplasms were diagnosed in 26 animals (Table 2). Twenty-five had been necropsied and one animal with a neoplasm was still alive at the end of the study. Eight felids had two different types of neoplasms diagnosed, and three felids had three separate neoplasia types (Table 2). Neoplasia involved the integumentary ( $n = 11$ ), endocrine ( $n = 10$ ), reproductive ( $n = 8$ ), hematopoietic-lymphoreticular ( $n = 5$ ), digestive ( $n = 3$ ), and hepatobiliary ( $n = 2$ ) systems (Table 3). One neoplasm remains unclassified by system.

Benign and malignant neoplasia types were of equal predominance with 10 types each. All hematopoietic-lymphoreticular tumors were malignant. Metastatic disease was observed in eight cats with five epithelial tumors and three round cell tumors. Metastatic tumors were as follows: three mammary adenocarcinomas, one exocrine pancreatic carcinoma, one carcinoma of unknown origin (carcinomatosis), two visceral mast cell tumors, and one lymphosarcoma. A total of 11 out of 19 (58%) female tigers and nine of 14 (64%) female lions in the study population had received MGA implants.

The ONR for the zoo felid population was 25% (26/103) and the NNR was 51% (24/47). One animal was cured of neoplasia and was later necropsied, and one animal was still alive at the end of the study. Cheetahs had the lowest SSR (11%) of felids, with only one specimen with neoplasia, and snow leopards had the greatest SSR (50%) (Table 1). The mean ( $\pm$  SD) age at death was  $14.8 \pm 4.1$  yr for all felids meeting the selection criteria, and the mean age at death for those with neoplasia at necropsy was  $15.8 \pm 3.4$  yr. The mean age for those animals where neoplasia was considered the cause of death was  $14.5 \pm 2.8$  yr. Neoplasia was determined to be the cause of death or euthanasia in 27% (13/47) of all the felids necropsied and 54% (13/24) of the zoo felids with neoplasia at necropsy.

Surgical resection was attempted in three animals. Resection was curative in a 15-yr-old tiger with seminoma and lymphangioma that died 2 yr after diagnosis with no neoplastic lesions observed at necropsy, and a 7-yr-old tiger with sebaceous gland adenoma that was still living in 2004. Surgery was not successful for one 16-yr-old tiger with a squamous cell carcinoma on the left rear limb.

**Table 2.** Neoplasia found in felids held at the Knoxville Zoological Gardens from 1979–2003.

Animal No.	Species	Age at time of death/age at time of diagnosis <sup>a</sup>	Sex	Primary system	Organ(s) affected	Diagnosis	Final outcome <sup>b</sup>
1	lion ( <i>Panthera leo</i> )	15.8	M	hepatobiliary	liver	biliary cystadenoma	OE
2	lion	19.2	M	hemolymphatic	spleen	lymphosarcoma	CE
3	lion	14.9	F	hemolymphatic	spleen, <sup>c</sup> bone marrow, bone marrow, liver, lymph nodes, urinary bladder	lymphosarcoma	CE
4	lion	19.3	F	reproductive	uterus	leiomyoma	OE
5	lion	16.7	F	reproductive	uterus	uterine adenocarcinoma	OE
				digestive	pancreas	exocrine pancreatic adenoma	OE
				reproductive	uterus	leiomyoma	OE
6	leopard ( <i>Panthera pardus</i> )	17.7	F	unknown	multiple metastasis	carcinomatosis	CE
				integumentary	mammary gland	mammary cystadenoma	OE
				endocrine	thyroid	thyroid cystadenoma	OE
7	leopard	18.3	M	reproductive	uterus	leiomyoma	CE
8	leopard	25.3	M	endocrine	thyroid	thyroid adenoma	OE
9	jaguar ( <i>Panthera onca</i> )	12.7	F	hepatobiliary	liver	cholangiocarcinoma	OE
				digestive	pancreas, <sup>c</sup> liver, mesentery	exocrine pancreatic carcinoma	CE
				integumentary	lymph node	squamous cell carcinoma	OE
10	tiger ( <i>Panthera tigris</i> )	15.7	F	integumentary	mammary gland	mammary adenocarcinoma	CE
11	tiger	14.6	F	integumentary	mammary gland	mammary adenocarcinoma	CE
				reproductive	uterus	leiomyoma	CE
				reproductive	uterus	uterine adenocarcinoma	CE
12	tiger	12.7	F	integumentary	mammary gland	mammary adenocarcinoma	CE
13	tiger	18/16	F	integumentary	skin	squamous cell carcinoma	OE
14	tiger	14	M	hemolymphatic	lymph node, <sup>c</sup> lung, liver	visceral mast cell tumor	OE
15	tiger	17.8	M	endocrine	parathyroid	parathyroid adenoma	OE
				endocrine	thyroid	thyroid adenoma	OE
16	tiger	14.9	F	integumentary	mammary gland, <sup>c</sup> uterus, ovary, vaginal, lung, liver, kidney, heart, adrenal, spleen, lymph nodes	mammary adenocarcinoma	CE
17	tiger	17.9/15.9	M	reproductive	testicle	seminoma	Diag
18	tiger	12.2	F	integumentary	subcutaneous	lymphangioma	Diag
				integumentary	mammary gland, <sup>c</sup> lymph nodes, lung, pleura, mediastinum	mammary adenocarcinoma	CE
19	tiger	10.7	F	integumentary	mammary gland, <sup>c</sup> lung, lymph nodes, liver, ovary, adrenal	mammary adenocarcinoma	CE
20	tiger	7	F	integumentary	skin	sebaceous gland adenoma	Diag
21	snow leopard ( <i>Panthera uncia</i> )	12.5	M	reproductive	testicle	seminoma	OE

Table 2. Continued.

Animal No.	Species	Age at time of death/age at time of diagnosis <sup>a</sup>	Sex	Primary system	Organ(s) affected	Diagnosis	Final outcome <sup>b</sup>
22	snow leopard	16.4	F	endocrine	thyroid	thyroid adenoma	PE-CH
23	bobcat ( <i>Felis rufus</i> )	9.6	M	endocrine	thyroid	solid thyroid carcinoma	PE
24	cougar ( <i>Felis concolor</i> )	17.3	F	endocrine	adrenal	adrenal adenocarcinoma	OD
25	cougar	18.4	M	hemolymphatic	pancreas	lymphosarcoma	CD
26	cheetah ( <i>Acinonyx jubatus</i> )	13.25	F	endocrine	thyroid	thyroid cystadenoma	OE
				digestive	adrenal	adrenal adenocarcinoma	OE
				hemolymphatic	thyroid	thyroid adenoma	OE
					pancreas	exocrine pancreatic adenoma	OD
					spleen, <sup>c</sup> larynx	visceral mast cell tumor, metastatic	OD

<sup>a</sup> When only a number is given, this indicates that the tumor was diagnosed at or near the time of death.

<sup>b</sup> Outcome abbreviations indicate what effect the tumor had on the animal. OE = euthanized due to other causes; CE = neoplasm cause of euthanasia; OD = other cause of death; CD = neoplasm cause of death; PE = possible cause of euthanasia or death; CH = cardiac hypertrophy (possibly secondary to functional thyroid tumor); Diag = diagnosis, still living or deemed cured.

<sup>c</sup> Presumed primary organ affected, when metastasis present.

This animal was euthanized 2 yr after surgery, due to declining quality of life as a result of a cervical cellulitis. The tumor had recurred and was ulcerated but was not considered by the pathologist or clinician to be the reason for euthanasia.

## DISCUSSION

Rates of neoplasia found in the present study are much greater than those found in the one comparable study.<sup>15</sup> Rates of neoplasia at felid necropsy in that study were 3.6% for 1901–1934 and 24.7% for 1935–1955,<sup>15</sup> compared with a 51% rate of neoplasia at necropsy for the Knoxville collection. Part of this increase is possibly due to our exclusion of very young animals from our study, but this does not seem to be the sole reason, because the Philadelphia report indicated that most of their animals were acquired later in life.<sup>15</sup>

Increased longevity due to better nutrition, management, and veterinary care would be a logical reason for the greater neoplasia rates in the Knoxville collection, but neoplasia did not appear to greatly affect the average age at death between the reports. In the latter time period (1935–1955) of the Philadelphia study, the mean ages of felids with neoplasia found at necropsy were 14.5 and 14.9 yr<sup>15</sup> of age for malignant and benign tumors, respectively, compared with a mean age of 15.8 yr for animals who had neoplasia at necropsy in the Knoxville collection.

It is also possible that environmental factors, particularly carcinogens, may play a role in the development of neoplasms in zoo felids. The Knoxville Zoological Gardens is located directly adjacent to a busy interstate highway in the middle of the city of Knoxville (population 173,890).<sup>26</sup> It seems possible that particulates and emissions from automobiles and other sources could play a role in cancer development in these felids. A comparison with a zoo in a more rural location, with known lower concentrations of potential carcinogens, would be ideal. High levels of automobile emissions are suspected to result in higher levels of neoplasia in humans and have been identified to contain carcinogenic properties in laboratory animals.<sup>18</sup> Carcinogens in cigarette smoke have been implicated as increasing domestic cats' risk of oral squamous cell carcinoma.<sup>2</sup>

A main clinical concern are those neoplasms that result in death or euthanasia. Neoplasia was identified as the cause of death or euthanasia in about half (13/24) of those felids that had neoplasia at necropsy, and only three neoplasms were diagnosed antemortem that did not result in death or euthanasia. In tigers, all six neoplastic causes of death

**Table 3.** Number of neoplasms found in a 24-yr retrospective of zoo felids classified by primary system involved and by species.

Species	System							Total
	Hemolymph	Endocrine	Digestive	Hepatobiliary	Integumentary	Reproductive	Unclassified	
<i>Panthera leo</i>	2	0	1	1	0	3	1	8
<i>Panthera pardus</i>	0	2	0	1	1	0	0	4
<i>Panthera onca</i>	0	0	1	0	1	1	0	3
<i>Panthera tigris</i>	1	2	0	0	9	3	0	15
<i>Panthera uncia</i>	0	2	0	0	0	1	0	3
<i>Felis rufus</i>	1	1	0	0	0	0	0	2
<i>Felis concolor</i>	0	3	0	0	0	0	0	3
<i>Acinonyx jubatus</i>	1	0	1	0	0	0	0	2
Total	5	10	3	2	11	8	1	40

or euthanasia were due to mammary neoplasms, and all six of these animals had been implanted with MGA. This tumor has been associated with the use of MGA contraception use, and the animals in the current study also were included in the report that investigated this association.<sup>11</sup> That study indicated that 94% of animals with mammary cancer had been given MGA and only 63% of nonaffected animals had been given MGA. Tigers had all six of the mammary adenocarcinomas in the collection. Uterine adenocarcinomas have also been associated with MGA treatment in zoo felids.<sup>20</sup> Both cats with uterine adenocarcinomas, one lion and one tiger, had been implanted with MGA.

Endocrine tumors were fairly common among the study group, with 10 out of 40 tumors originating from endocrine organs. Most of these tumors were of thyroid origin, with one carcinoma, four adenomas, and two cystadenomas. Thyroid tumors and thyroid hyperplasia are important causes of hyperthyroidism, often resulting in clinical disease in domestic cats.<sup>7,25</sup> One snow leopard in the current study with thyroid adenomas and a thyroid carcinoma also had cardiac hypertrophy with pleural effusion and pulmonary edema. Because hyperthyroidism has been linked to cardiac hypertrophy in domestic felids, hyperthyroidism may have been the cause of the declining condition of this animal.<sup>14</sup> The large incidence of thyroid tumors in this collection may warrant further investigation and comparison to other collections to see if risk factors can be determined. Thyroid tumors also have been reported in other zoo felids.<sup>10,22,23</sup> In one time period (1935–1955) of a previous study, four out of all eight felids with neoplasms had thyroid carcinomas, which was believed to be linked to the lack of iodine supplementation.<sup>15</sup> Numerous potential etiologies have been suggested for hyperthyroidism in domestic felids with no definitive cause identified.<sup>7</sup>

Hematopoietic tumors included two visceral mast cell tumors and three lymphosarcomas, both of which have been reported previously in several zoo felids.<sup>3,8,10,16,17</sup> The visceral mast cell tumors in the current study both had metastatic lesions. Visceral mast cell tumors are not commonly reported in domestic felines,<sup>1</sup> but lymphosarcoma is common.<sup>4</sup> Lymphoma in domestic felids is associated with infection by feline leukemia virus (FeLV) and feline immunodeficiency virus (FIV), and FeLV has been reported to be a possible cause of lymphoma in a lion and cheetah.<sup>6,16,24</sup> FIV has been associated with lymphoma in a lion as well.<sup>21</sup> In this current study, the bobcat with lymphosarcoma was seropositive for FeLV. One lion was FeLV positive by ELISA but FeLV negative by bone marrow immunofluorescent antibody (IFA) 2 yr prior to diagnosis of lymphosarcoma. At that time the animal had splenomegaly, myelophthisis, and anemia. At the time of diagnosis of lymphoma, 2 yr after the initial onset of symptoms, the animal tested negative for FeLV by ELISA, IFA, and virus isolation. The other lion with lymphoma was not tested for FeLV or FIV. Alternatively, lymphoma may have arisen spontaneously in these animals, or it may have been associated with other carcinogenic factors.

Snow leopards had the highest incidence of neoplasia (50% SSR, 100% SSNR) in the population. This cannot be completely explained by an increase in mean age (14.5 yr) for snow leopards, because other species with higher mean ages at death (leopard, 19.8 yr, and lion, 15.4 yr) had lower neoplasia rates (33% and 19%, respectively). Cheetahs and jaguars had low rates of neoplasia (SSR = 11%, SSNR=33% and SSR=17%, SSNR=33%, respectively). It is possible that the earlier death ages of these animals (mean ages at death = 12.7 and 11.8 yr, respectively) resulted in lower neoplasia rates. However, the populations of jaguars, snow leopard,

ards, and cheetahs were relatively small, so the rates may not be characteristic of a larger population.

Multiple neoplasms were detected in 11 felids, with most of these representing the most common systems involved in all neoplasms in this study. However, all felids with pancreatic tumors, which were rare overall, had at least one other type of neoplasm. Multiple neoplasms have been reported previously in several zoo felids, and the current results show that this is not a rare occurrence.<sup>5,13,22</sup>

The current study could determine only baseline trends in the types and incidence of neoplasms at the Knoxville Zoo. Some risk factors for development of neoplasms in zoo felids have been discussed and concerns have been raised about the number of neoplasms in the collection. Future studies may include comparison with other zoo collections to compare types and incidences of neoplasia and may attempt to identify risk factors involved in neoplasia development.

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