

## Incidence of spontaneous tumours in guinea pigs: a retrospective study of 153 cases

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### Abstract

The aim of this study was to investigate the incidence of spontaneous tumours in guinea pigs in biopsy and necropsy samples in the monitored period (2016–2022) on a representative number of cases and to determine their occurrence in relation to age and sex of the animals. A total of 204 samples from various pathological lesions were examined, while 153 cases (75.00%) were true tumours and 51 cases (25.00%) were pseudotumorous non-neoplastic lesions. The distribution of the incidence of true neoplasms in relation to sex was uneven. In the examined group, more neoplasms were diagnosed in males ( $n = 88$ , 57.52%) compared to females ( $n = 65$ , 42.48%). The mean age of guinea pigs with diagnosed tumour in our group was 4.2 years. Thyroid adenocarcinoma was the most frequent tumour. The majority of thyroid tumours (67.86%) were diagnosed in animals aged 4–5 years, as a significant result in terms of incidence in this age range, as well as a predisposition to tumour formation in males (78.57%). Mammary gland tumours occurred in the age range of 2–7 years, with a mean age of incidence of 4.7 years. In all cases, these were malignant variants and showing a significant higher incidence in males, in the age range of 4–5 years. The processing of a representative number of samples and epidemiological data on the incidence of spontaneous tumours in guinea pigs can contribute to the overall expansion of knowledge about this topic in veterinary medicine.

*Rodents, histopathology, neoplasia, prevalence, thyroid gland, mammary gland*

Current knowledge about spontaneous tumours occurring in captive pet guinea pigs is rather scarce. Although various types of lesions have been described in a number of individual case reports, comprehensive studies including all types of neoplasia in all organ systems, including the age of the animals, are not routinely performed. Therefore, the prevalence and age distribution of most tumour types is largely unknown. Compared to another very popular small pet animal, the domestic rabbit (*Oryctolagus cuniculus*), information available on the occurrence of spontaneous tumours in guinea pigs (*Cavia porcellus*) is rarer. According to available literary sources, spontaneously occurring neoplasms in guinea pigs are not frequent. They usually occur in animals older than 3 years, but can appear as early as at 4 months of age (Rogers and Blumenthal 1960; Jelínek 2003; Greenacre 2004; Jenkins 2010). Commonly described tumours in this species include bronchogenic papillary adenoma, trichofolliculoma, various types of other cutaneous tumour, fibroadenomas and adenocarcinomas of the mammary gland. Different uterine tumours have also been described (Kitchen et al. 1975; Rao et al. 1980; Field et al. 1989). The aim of this study was to investigate the incidence of spontaneous tumours in guinea pigs on a representative number of samples in relation to their age and sex.

### Materials and Methods

Tissue samples intended for histopathological examination were obtained from the biopsy and necropsy material of the Department of Pathological Morphology and Parasitology, University of Veterinary Sciences Brno, in the monitored period from 2016 to 2022. The samples came from the clinical workplaces of the university

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and from field veterinary workplaces in the Czech Republic. A total of 204 different lesions were examined in guinea pigs. All tissue samples were fixed in 10% buffered formalin and routinely processed. Subsequently, 4 mm sections were made and stained with haematoxylin and eosin (HE) for evaluation of lesions. In a few cases, where determination of definitive diagnosis based on HE stain was not clear, immunohistochemical examination was used. In such a case, tissue sections were prepared on special glass slides with an adhesive layer with a permanent SuperFrost® charge (Thermo Fisher Scientific, Waltham, USA). After deparaffinization in xylene and hydration in alcohol series, a buffer with an appropriate pH was used to unmask surface receptors. Primary antibodies used: polyclonal rabbit anti-human CD3 (Dako, Glostrup, Denmark), prediluted antibody; polyclonal rabbit anti-human CD20 (Thermo Fisher Scientific), dilution 1:50; monoclonal mouse anti-human cytokeratin (clone AE1/AE3) (DCS, Hamburg, Germany), dilution 1:100; monoclonal mouse anti-human SMA (smooth muscle actin, clone 1A4) (Dako), dilution 1:50; monoclonal mouse anti-human S-100 protein (clone IHC110) (DCS), dilution 1:100; monoclonal mouse anti-human melan A (clone A103) (DCS), dilution 1:50; polyclonal rabbit anti-human CD117, c-kit (Dako), dilution 1:100; monoclonal mouse anti-human chromogranin A (clone 5H7) (Leica Biosystems, Wetzlar, Germany), dilution 1:50; monoclonal mouse anti-human vimentin (clone V9), (DCS), dilution 1:100. EnVision+ System HRP (Labeled Polymer) Detection System (Dako) was used. Commercial solutions were used to dilute the primary antibodies. The data were statistically analysed (software STATISTICA CZ Version 12, StatSoft, Czech Republic; *P* values < 0.05 were considered significant). The results were mentioned when significant.

## Results

In this study, a total of 204 biopsy and necropsy samples from various pathological lesions in guinea pigs were examined, while 153 cases (75.00%) were diagnosed as true tumours. In 51 individuals (25.00%), it was a pseudotumorous non-neoplastic lesion, macroscopically imitating neoplastic proliferation (e.g. granulomatous panniculitis, cystic degenerative changes of the ovaries, reactive fibroplastic tissue, haematomas, focal hypertrophy of the uterine wall and others). The distribution of the incidence of true neoplasms in relation to sex was uneven. In the examined set of samples, more neoplasms were diagnosed in males at a total of 88 tumours (57.52%), whereas in females a total of 65 tumours (42.48%) were found. As pets, guinea pigs live for an average of 6–8 years. The mean age of the guinea pigs with a diagnosed tumour in our set of examined samples was 4.2 years, with the majority of the guinea pigs belonging to the age category of 3–5 years.

Out of a total of 153 diagnosed tumours, adenocarcinoma of the thyroid gland was the most frequently represented one in the examined group at 18.30% (*n* = 28). The occurrence of lipomas ranked second with a representation of 16.34% (*n* = 25). Other tumours with more frequent occurrences were soft tissue cutaneous and subcutaneous sarcomas (fibrosarcoma, myxofibrosarcoma, myxosarcoma) with a representation of 13.72% (*n* = 21 lesions). Other more frequent tumours were adenocarcinoma of the mammary gland, which occurred in 11.76% of cases (*n* = 18) and lymphoma in 10.46% of cases (*n* = 16). Other detected lesions were represented by benign trichoepithelioma (4.57% of cases, *n* = 7), uterine leiomyosarcoma (3.92% of cases, *n* = 6), uterine adenocarcinoma (3.28% of cases, *n* = 5). Other neoplasms diagnosed in the investigated group included those with less frequent occurrence: splenic haemangiosarcoma (1.96% of cases, *n* = 3), trichofolliculoma (1.31% of cases, *n* = 2), malignant trichoepithelioma (1.31% of cases, *n* = 2), cutaneous squamous cell carcinoma (1.31% of cases, *n* = 2), subcutaneous liposarcoma (1.31% of cases, *n* = 2), gastrointestinal stromal tumour of the caecum (1.31% of cases, *n* = 2), lung adenocarcinoma (1.31% of cases, *n* = 2). The tumours that were detected in individual cases in the examined set of samples comprised cutaneous haemangioma, fibroma, subcutaneous haemangiosarcoma, angioliipoma, gastric leiomyosarcoma, pancreatic insulinoma, hepatocellular adenoma, testicular seminoma, ovarian granulosa cell tumour, lacrimal adenocarcinoma, oral cavity papilloma and thyroid gland adenoma. The incidence of individual types of neoplasms in the examined set of samples (*n* = 153), the mean age of occurrence, and the representation by sex are summarized in Table 1.

Table 1. Incidence of tumour types (n = 153), mean age of occurrence, and distribution by sex.

Tumour	Biopsy		Mean age Years	Female Number	Male Number
	Number	%			
Thyr AC	28	18.30	4.4	7	21
Lipoma	25	16.34	3.4	11	14
STS	21	13.72	5.0	11	10
Mm AC	18	11.76	4.7	4	14
Lym	16	10.46	3.9	8	8
TE (b)	7	4.57	3.7	4	3
LS (u)	6	3.92	3.5	6	0
AC (u)	5	3.28	3.6	5	0
HS (spl)	3	1.96	3.8	2	1
TF	2	1.31	3.5	1	1
TE (m)	2	1.31	4.0	0	2
SCC	2	1.31	4.5	1	1
Lsarc	2	1.31	3.5	1	1
GIST	2	1.31	5.5	1	1
Ln AC	2	1.31	4.5	0	2
H	1	0.65	4.0	0	1
HS (sub)	1	0.65	6.0	0	1
AngioL	1	0.65	3.0	0	1
Fibroma	1	0.65	3.0	1	0
LS (g)	1	0.65	4.0	0	1
Ins	1	0.65	5.0	0	1
HC aden	1	0.65	6.0	1	0
Sem	1	0.65	4.0	0	1
GCT	1	0.65	3.0	1	0
Lac AC	1	0.65	6.0	0	1
Pap	1	0.65	4.0	0	1
Thyr A	1	0.65	4.0	0	1
Total	153	100	4.2	65	88

Thyr AC – thyroid gland adenocarcinoma, STS – soft tissue sarcoma, Mm AC – mammary gland adenocarcinoma, Lym – lymphoma, TE (b) – benign trichoepitelioma, LS (u) – uterine leiomyosarcoma, AC (u) – uterine adenocarcinoma, HS (spl) – splenic haemangiosarcoma, TF – trichofolliculoma, TE (m) – malignant trichoepitelioma, SCC – squamous cell carcinoma, Lsarc – liposarcoma, GIST – gastrointestinal stromal tumour, Ln AC – lung adenocarcinoma, H – haemangioma, HS (sub) – subcutaneous haemangiosarcoma, AngioL – angiolioma, LS (g) – gastric leiomyosarcoma, Ins – pancreatic insulinoma, HC aden – hepatocellular adenoma, Sem – seminoma, GCT – ovarian granulosa cell tumour, Lac AC – lacrimal adenocarcinoma, Pap – oral cavity papilloma, Thyr A – thyroid gland adenoma

Thyroid adenocarcinoma occurred in the age range of 2–8 years, with a mean age of incidence of 4.4 years. The vast majority of these tumours (67.86%) were diagnosed in animals aged 4–5 years, and this was a significant result in terms of incidence in this age range, as well as a predisposition to tumour formation in males (78.57%) (21 adenocarcinomas and 1 adenoma). Cutaneous and subcutaneous neoplasms made up a significant part of all diagnosed lesions (42.48%). Melanocytic tumours were not represented at all in the examined set of samples. No age or sex predisposition was found for any of the neoplasms. Mammary gland tumours occurred in the age range of 2–7 years,

with a mean age of incidence of 4.7 years. In all cases, these were malignant variants (adenocarcinomas). In our examined material no histologically benign variant of the tumour was detected. In our group a significantly higher incidence of neoplasms was found in males, in the age range of 4–5 years. In case of lymphomas (10.46%), both sexes were equally represented, the mean age of occurrence in this group was 3.9 years, the tumour occurred in the age range of 2–7 years. Other neoplasms were represented with a lower frequency.

## Discussion

The most frequently diagnosed tumour was adenocarcinoma of the thyroid gland. Sex predisposition to the development of thyroid neoplasms in guinea pigs has not yet been studied. A benign variant of the neoplasm, a solid-cystic adenoma of the thyroid gland, was diagnosed in only one case in the monitored group. Histologically, adenocarcinomas were mainly formed by papillary or tubulopapillary proliferating cubic cells. Cellular atypia was slightly to moderately pronounced in most of the neoplasms. In five cases, foci of ossification/bone metaplasia of varying intensity were detected within the stroma of the neoplastic tissue. The relatively high incidence of thyroid gland tumours in investigated group differs from other available data. However, it should be noted that information on the occurrence of spontaneous tumours in guinea pigs compared to other pet animals is rather rare. Therefore, the prevalence and age distribution of most tumour types in guinea pigs is largely unknown. This is also why endocrine tumours in guinea pigs are rarely described, and only endocrine disorders such as functional ovarian cysts have been comprehensively described in this species (Keller et al. 1987; Beregi et al. 1999; Shi et al. 2002; Nielsen et al. 2003). In the last decades, case reports have been published describing tumours of the thyroid gland, adrenal glands and pancreas (Gaschen et al. 1998; Vannevel and Wilcock 2005; Gibbons et al. 2013). Generally, the higher incidence of endocrine tumours in guinea pigs in the recent period described in case reports may be related to the earlier lower availability of practical information on the diagnostic procedures for these conditions and, at the same time, the higher level of acquired knowledge about these diseases at present (Zeugswetter et al. 2007; Mayer et al. 2010; Künzel et al. 2013). For the above reasons, the prevalence of thyroid neoplasms in guinea pigs may have been underestimated in the past. In one study, thyroid neoplasms were found in 3.6% of all cases of guinea pig biopsies for histopathological examination (Gibbons et al. 2013). Thyroid tumours can be associated with hyperthyroidism, but they can also be non-functional in guinea pigs (Zarrin 1974; LaRegina and Wightman 1979; Pignon and Mayer 2013). Cutaneous and subcutaneous tumours (42.48%) represented a significant part of the diagnosed lesions in the examined group. The most common tumour of epithelial origin was trichoepithelioma, of mesenchymal origin adipose tissue neoplasm (lipoma and liposarcoma), followed by other soft tissue tumours (fibrosarcoma and myxofibrosarcoma). No age or sex predisposition was found for any of the detected neoplasms. Lipoma had the most frequent occurrence in the subcutaneous tissue in the mammary gland and inguinal area. Soft tissue sarcomas were on average detected in older animals (5.0 years) with predominant location on the back and side of body. The obtained results are consistent with some available literature data on these neoplasms (Kanfer and Reavill 2013). In contrast, some authors report that skin neoplasia is significantly more often diagnosed in guinea pigs younger than 2 years of age (Minarikova et al. 2015). According to these studies, the vast majority of skin neoplasms belong to the category of benign tumours. Previously, the most frequently described skin tumour was trichofolliculoma (Greenacre 2004; Garner 2007; Kanfer and Reavill 2013; Hocker et al. 2017). However, this lesion was represented in only 2 cases in our group. Some authors report a higher incidence in females

(Otrocka-Domagala et al. 2022), whereas other studies indicate a higher incidence in males (Garner 2007; Hawkins and Bishop 2012). All cases of mammary gland tumours involved adenocarcinomas, no benign variant was detected. The predominance of neoplasms was found in males in our group, especially in the age range of 4–5 years. The majority of tumours were histologically simple, and included mainly tubulopapillary, then tubular or intraductal papillary forms. Mammary gland tumours are described in both female and male guinea pigs, with the prevalence in relation to sex varying between studies, some reporting an approximately equal distribution in males and females, some reporting a higher incidence in males or females (Andrews and Shively 1976; Greenacre 2004; Saba et al. 2007). Similar to other species, these tumours can develop in guinea pigs due to the effects of oestrogen and progesterone (Suarez-Bonnet et al. 2010). In general, it can be stated that the incidence of mammary gland neoplasms in male guinea pigs is significantly higher compared to other animal species. Lymphoma was detected in 10.46% of cases. Of these, 2 cases involved lymphoma diagnosed from biopsy material (lymph nodes), and 14 cases involved necropsy material with generalized disease and involvement of multiple organ systems. Histologically, pleomorphism and predominantly higher mitotic activity of neoplastic cells were detected. Immunophenotypically, most cases were T-cell lymphoma. Both sexes were equally represented. The obtained results are in accordance with the available literature data (Hong et al. 1980; Debout et al. 1987; Steinberg 2000; Kolodziejaska et al. 2010), although some sources report a lower incidence of this neoplasia in guinea pigs compared to other animal species, explaining this fact by the presence of an enzyme with L-asparaginase activity discovered in guinea pig serum, leading to “starvation” of neoplastic cells (Schalk et al. 2014). Lymphoma has also been experimentally induced in guinea pigs secondary to chronic antigen stimulation (Ziegler and Ziegler 1994). Other tumours in our group were represented with a lower frequency.

The processing of a representative number of samples and epidemiological data on the incidence of spontaneous tumours in guinea pigs can contribute to the overall expansion of knowledge about this topic in veterinary medicine.

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