# TDK THESIS

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# Comparing histopathological results of 28 biopsy samples from small exotic mammals – guinea pigs *(Cavia porcellus)*, rabbits *(Oryctolagus cuniculus)*, rats *(Rattus norvegicus domesticus)*, and a hamster *(Mesocricetus auratus)* with presenting clinical signs.

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## List of Abbreviations

| | |
|---|---|
| GP | Guinea Pig |
| RB | Rabbit |
| RT | Rat |
| HM | Hamster |
| SEM | Small Exotic Mammal |
| CS | Clinical Sign |
| CEH | Cystic Endometrial Hyperplasia |
| HP | Hyperplasia |
| UB | Urinary Bladder |
| MG | Mammary Gland |
| SC | Subcutaneous |

# 1. Introduction

## 1.1. Small Exotic Mammal Pets

Small Exotic Mammals (SEM) are growing more common as family pets [2, 3, 29, 69]. In the United States, SEMs are the fourth most owned household pets after dogs, cats, and freshwater fish, [1] but continue to be underrepresented in the field of Veterinary Medicine. For instance, university students overlook how frequently these critters visit clinics for routine examinations and emergencies; therefore, they choose to not focus on the subject properly. Additionally, working veterinarians do not consider how different the presenting clinical signs (CS), lesions, and potential diseases are in SEMs, versus a dog or a cat. For example, SEM are prey, therefore, they hide signs of disease to avoid being attacked by a predator, while dogs and cats, as predators, typically show signs at the beginning of illness [4]. A recent study done by Wills and Holt in 2020 reported that veterinarians in the UK were significantly less confident treating and diagnosing rabbits (RB), guinea pigs (GP), and small rodents in comparison to cats and dogs [12]; although 30% of the vets surveyed mentioned seeing at least one RB daily [12]. This further proves that Veterinarians receive limited training to care for such animals, which later affects their confidence in the field [4] and therefore, misdiagnosis and improper treatment of SEMs can occur. Lastly, SEM disease research is sparse, and outdated [3], and further contributes to misdiagnosis because Veterinarians do not have enough trustworthy sources.

SEMs include, but are not exclusive to, rats (RT), RBs, and hedgehogs. However, in this paper, SEM will refer directly to guinea pigs (*Cavia porcellus)*, rabbits (*Oryctolagus cuniculus domesticus)*, rats (*Rattus norvegicus domesticus*), and Syrian hamsters (HM) (*Mesocricetus auratus*).

## 1.2.Goal of the Study

The goal of this study is to compare the histopathological results of lesions from varying tissue in SEM pets: GPs, RBs, RTs, and Syrian HMs with their presenting CSs. Specifically, to bring awareness to SEMs and their individuality when it comes to specific species disease diagnosis.

## 2. Literature Review

### 2.1. Advantages of Histopathology

Histopathology is a diagnostic method based on examining tissue sections under a microscope. It is considered the "gold standard" for tumor diagnosis and looks at different processes of the tissue [5]. Additionally, it is important for determining potential causes of diseases and staging the severity of neoplasms.[5]. For instance, it is the only method that can grade the malignancy of a tumor [7]. Therefore, it helps veterinarians create proper treatment plans and let owners know what to expect in terms of prognosis.

### 2.2. Histopathology Methods

To receive accurate histopathology results, certain steps are taken. The tissue must be properly sampled, trimmed, fixed, and prepared [6,7]. If evaluated or processed in a different facility, then biopsied and shipped properly for accurate results [6,7]. Different biopsy methods exist including, but not exclusive to, wedge biopsy, cutaneous punch biopsies, endoscopic collection, and surgical excision [8]. The biopsy technique used will depend on the size and location of the mass, and the personal preference of the veterinarian [8].

#### *2.2.1. Incisional Biopsy*

This is a common biopsy method. Incisional biopsies describe the process where samples are taken from a smaller portion of the affected area [7, 8].

#### *2.2.2. Excisional Biopsy*

An excisional biopsy removes the entire lesion along with a part of the normal tissue in the area [7, 8]. Excisional biopsies are preferred in case of malignant and smaller-sized lesions, and if a mass is suspected to be cancerous [8]. These are larger surgical treatments.

### 2.3. Reasons For Histopathology Studies

Since SEMs are becoming more common household pets, veterinarians need to be able to relate lesions to possible diseases and CSs to make a proper diagnosis. In most cases, the earlier the disease is discovered and diagnosed the better the prognosis. And using histopathology can help make that happen. Research comparing different SEM diseases and histopathology is small, but fortunately a growing field. Articles comparing single organ systems, [3, 13, 15], only neoplastic processes [19], or only a single species do exist [10, 17, 26, 70]; however, this makes it difficult for veterinarians to have a bigger picture of possible diseases in varying species and organs. A couple of studies do exist which give an overview of possible spontaneous lesions in multiple species [3, 11] but fail to reflect on different

clinical presentations: systemic or local. In this paper, neoplastic and non-neoplastic lesions are compared. Neoplastic lesions in this study are spontaneous, which means they developed naturally, not via laboratory methods. This comparison of histopathological results in SEMs and their presenting CSs gives veterinarians broader knowledge of commonly visiting exotic mammals' potential diseases and CSs.

### 2.4. Guinea Pig Lesions

#### 2.4.1. Lesions of the Reproductive Tract

Current research that gives a broad overview of changes to the reproductive tract of GPs is sparse. A plethora of studies looked at specific diseases, such as cystic rete ovarii [25, 32, 33, 73, 74] reports on single GP cases [26], or discuss trials for human medicine on laboratory animals [47, 50]. Overall, female reproductive tracts have been one of the most researched organ systems in GPs; specifically, the uterus was reported to have the highest incidence of lesions [26 – 30, 32, 33, 73, 77, 78]. Research on male GP reproductive tracts was significantly less abundant. Only two cases of testicular tumors – seminoma [68] and embryonal carcinoma [68, 82, 83] - exist. Studies found the older the GP the greater the probability of genital tract disorders [28, 29, 31]. A retrospective study done by Bertram and others in 2018 compared 655 samples from the reproductive tract and reported that 77.8% of pet GPs were affected over the age of six years [28]. This study was based mostly on necropsies, [28] thus, it is important to consider that the age range may be skewed because the GPs have all passed. In addition, studies reported that different uterine lesions affected different ages of GPs. Uterine neoplasia and hyperplasia (HP) increased with age, and uterine inflammation was highest in GPs between seven to twelve months of age [28]. Neoplastic uterine alterations were reported in GPs older than three years of age [29, 31], and ovarian cysts over one-and-a-half years [25]. Past studies claimed that tumors and non-neoplastic lesions of the female genital tract were uncommon [27, 29]. However, recent studies found that GPs over three years of age were affected by as much as 30% of neoplastic alterations in the uterus [31]. The increase in neoplastic lesions was believed to be because GPs are becoming common pets and no longer only laboratory animals [29]; thus, due to longer lifespans, there was a greater chance of developing such diseases. Multiple studies reported that the most common uterine neoplasia diagnosed was uterine leiomyomas – which can make up to 46% of the neoplastic changes in the uterus [20, 27 - 30]. Leiomyomas were often found concurrent with cystic rete ovarii [27]. Other possible uterine neoplasms reported were cavernous hemangioma [28, 30], adenoma [28, 29], anaplastic tumors [29],

teratomas [30], leiomyosarcoma [28, 29], and deciduosarcoma [28]. In the ovaries, the most common neoplastic change reported was a teratoma [11, 20, 57]. Veiga-Parga and others in 2016 claimed that 69% of the studied GP population was affected by cystic endometrial hyperplasia (CEH), a non-neoplastic lesion [29]. In comparison, a study claimed that uterine inflammation was the most common non-neoplastic lesion followed by endometrial HP [28]. The difference in results may be due to the number of GPs reviewed in each study and that one study reviewed mostly autopsy results, while the other looked significantly more at biopsy samples. A significant non-neoplastic lesion frequently discovered in the ovaries was ovarian cysts. [18, 20, 25, 28 - 30 32, 33, 70, 73, 74]. They were claimed to be as common as 22% in living pet GPs [18] and 78% postmortem [25, 32]. There have been five identified ovarian cysts [25, 33]. The three most common, in descending order, are serous cysts, also known as cystic rete ovarii, follicular cysts, and parovarian cysts. [25, 33]

Studies lack direct comparisons of GPs presenting CSs at the time of sample taking to the different neoplastic and non-neoplastic diagnoses. Often the researchers only cover the ages and genders of the animals, but some studies list general CSs for veterinarians to pay attention to. For example, GPs presenting with abdominal distention, a palpable mass, vaginal discharge, and/or abdominal pain shall have uterine and ovarian tumors included on their differential diagnostic list [20, 51]. As for cystic ovarian disease, non-pruritic, bilateral, symmetrical alopecia, enlarged external genitalia, and/or hyperkeratotic teats have been reported [18, 25, 33, 57]. In addition, non-specific CSs such as lowered body condition, lethargy, and abdominal pain might be recorded in some of the GPs [18, 25, 33]. The studies, however, did not discuss how common the non-specific signs were.

#### 1.1.1. Lesions of the subcutaneous and cutaneous tissue

Externally palpable masses were frequently reported in GPs. Ages ranged based on the diagnosis of the subcutaneous (SC) and cutaneous mass. For instance, lipoma was reported to affect slightly younger animals; however, on average SC and cutaneous lesions were reported in three-year-old GPs, but could affect any age [3, 18, 19, 24]. Reports agreed that male and female GPs were similarly affected by SC and cutaneous tumors [19, 24]. A study by Dobromylskyj and others in 2023, reported that the most frequent externally palpable mass arises from the SC and cutaneous tissue making up 88.9% of GP lesions [24]. Following far behind were mammary gland (MG) tissue and thyroid gland masses [24]. This portion excludes MG and thyroid gland tissue findings, but in the following section MG lesions will be discussed. Since GPs are common household pets, seeing a cutaneous tumor

in a clinic is not uncommon [3, 21] A study done by Otrocka-Domagala in 2022 reported that histopathological results of the epithelial tissue were mostly neoplastic and originated from adipocytes or fibroblasts, with lipoma being the most frequent diagnosis [3]. However, this conflicted with most researchers who claimed that trichofolliculoma was the predominant cutaneous tumor identified [11, 18-20, 34, 51, 58, 71]. Minarikaova and others in 2015 even discovered that 89.7% of skin tumors were trichofolliculoma [18]. A few other cutaneous neoplasms reported were lipoma [11, 18, 19], trichoepithelioma [11, 19], sebaceous adenoma [11, 18, 19], fibrosarcoma [11, 18, 19, 49], and liposarcoma [19, 48, 50-52]. Studies agreed that benign growths were more common in GPs than malignant masses [3, 18, 19, 21, 34]. Although neoplastic growths predominated in the SC and cutaneous tissue; non-neoplastic alterations such as hyperplastic changes, inflammatory processes, cysts, and hamartomas have also been reported [24].

The only frequently reported CS was a superficially palpable and visible mass for SC and cutaneous lesions [24].

Systemic CSs were not recorded by studies. However, Kanfer and Reavill in 2013 discussed the visual appearance and location of trichofolliculoma and lipomas. For example, he noted that trichofolliculomas were mostly located dorsal-caudal in the lumbosacral area and were large [11, 18, 19]; but can occur anywhere on the body [19]. Although trichofolliculoma is a benign growth, it has been reported to rupture and ooze either a white or gray thick sebaceous discharge and may ulcerate [19]. Lipoma masses feel soft to firm and can be located anywhere on the body; [19] however, they were predominately reported on the ventral abdomen [19].

#### 1.1.2. Lesions of the Mammary Gland Tissue

Studies reported that approximately 30 to 66% of MG tumors localized in GPs were malignant [19, 20, 51, 57]. The most identified malignant MG tumors in GPs were adenocarcinomas [19, 20]. Researchers claimed that MG gland adenocarcinomas were the third most frequent palpable mass identified in GPs. [19, 20]. The most frequently identified benign neoplastic proliferation in the MG tissue reported were adenomas [19, 20, 57]. Other lesions found in the MG tissue or near the MG tissue include mastitis and lipomas [19, 20, 51].

In comparison to the other animals discussed, GPs were one of two species where males were also affected by MG alterations [19, 20].

CSs were not discussed in the previous studies.

## 1.2.Rabbit Lesions

### 1.2.1. Lesions of the Reproductive Tract

In RBs, the uterus was the most frequently reported reproductive organ biopsied for histopathological review [36]. Lesions in the ovaries, fallopian tubes, vagina, and testicles have also been reported but were less significant [10, 36]. Studies report that uterine neoplasm incidences increase with a RB's age [36]. It is also reported that CEH can coincide with uterine neoplasia; however, CEH is reported to affect slightly younger RBs [38]. RBs with CEH were claimed to be mid-aged and the incidences increased with age [38]; however, a single study discovered a four-month-old RB with CEH [46]. Uterine inflammation was reported in RBs ages two to four years, significantly younger than neoplastic and HP changes [36]. A study done by Bertram and others in 2018 claimed that 510 different uterine disorders exist in RBs, with uterine neoplasms being the most frequent finding [36]. A couple of studies had similar claims [10, 40], while other studies reported endometrial HP as the most common uterine lesion [37, 38] The most frequently reported neoplasm in RBs was uterine adenocarcinoma [10, 36, 40]. Additionally reported, but infrequent neoplasms of the uterus were leiomyoma [37, 47] and leiomyosarcoma [37, 38], cavernous hemangioma [38], malignant mullerian tumor [42, 43], deciduosarcoma [44], and choriocarcinoma [45]. Non-neoplastic lesions of the reproductive tract mentioned were genital tract polyps [35, 37], hydrometra [37, 40], endometrial venous aneurysm [39, 40], and most predominantly cystic and non-cystic endometrial HP [37, 38, 40, 41, 46, 55]. Two studies reported that endometrial HP was the second most frequent reproductive tract lesion in RBs, followed by uterine inflammation [36, 40]. Male RB genital tract lesions were reported less, but neoplasms described include granular cell tumors [10, 66], testicular gonadoblastoma [59], seminoma [62, 63, 66], Sertoli cell tumor [10, 65, 66], mixed cell-type tumors, [63, 65, 66] myofibroma, [64] and interstitial (Leydig) cell tumor [60, 63]; and a non-neoplastic lesion reported infrequently was testicular atrophy [67]. A study reported that the most common testicular lesions were granular cell tumors [10].

CS reported in previous studies include inflammation coinciding with purulent discharge [37], serosanguineous discharge coinciding with endometrial HP [40], and endometrial venous aneurysms rupturing in younger animals resulting in bloody vaginal discharge [39].

### 1.2.2. Lesions of the Mammary Tissue

MG tissue lesions have been frequently reported in RBs [10, 14, 15]. Since RB husbandry has improved, RBs live longer and have been reported to develop such diseases more often,

specifically neoplasms [14]. Previous studies reported that RBs over six years have the highest frequency of MG tumors [10] and the mean age reported was between 4.9 and 5.5 years (age range: 8 months to 14 years) [13-17, 23]. A single study reported that the mean age of RBs with carcinomas was significantly higher than those of adenomas [15]. Baum and others in 2015 reviewed 109 MG masses and reported that 88% of the samples were malignant neoplasms [15], and an additional study found that 94% had malignant histological features [22]. The most frequent neoplasms reported were varying types of carcinomas [10, 15, 16, 23]. The studies reported that the most frequent non-neoplastic proliferative lesions of the MG tumor were cysts [16, 23]. Additional non-neoplastic proliferations reported in a RBs MG tissue include lobular HP, fibroadenomatous HP, and cystic duct ectasia [14-16]. Benign neoplastic lesions in the MG tissue such as adenomas, intraductal papillary adenomas, and papillomas were infrequent but reported [15, 22, 23].
The involvement of cranial and caudal MG was equally reported [15]. CSs of MG tumors reported in studies were few, but secretory activity and uterine adenocarcinoma were noted to sometimes coincide with MG neoplasm or HP [15, 23, 84]

### 1.3. Rat Lesions

#### 1.3.1. Lesions of Cutaneous and Subcutaneous Tissue

RTs have been commonly reported to have dermatological diseases [21, 52, 71]. The mean age RTs were reported to be affected by SC and cutaneous lesions was 1.8 years old [3]. White and others in 2019 compared lesions of companion rats and the most frequently discovered lesions were neoplastic and located in the SC tissue [71]. That study excluded the histopathological results for SC lesions [71]. From the cutaneous results, the most common neoplasm diagnosed in RTs was squamous cell carcinoma, followed by fibroma [71]. In contrast, a study that looked at both SC and cutaneous lesions diagnosed soft tissue sarcomas as the most frequent lesion [3]. Unique to RTs are zymbal glands, which are special auditory sebaceous glands located ventral to the external ear orifice [20, 55]. Studies reported that these glands can be affected by SC masses and that their histopathological results come back as malignant carcinomas or less frequently adenomas [20, 55, 56, 72]. Other differential diagnoses for Sc and cutaneous lesions reported were mites and Demodex, these have been reported in histopathological results and to cause noticeable tissue lesions [71].
No potential CSs were reported in past studies looking at SC and cutaneous lesions in pet RTs.

#### 1.3.2. Lesions of Mammary tissue

MG tumors have been frequently reported lesions in RTs [71, 85]. Similarly, to GPs, MG tumors were reported to occur in both female and male RTs [20, 57]. The most reported tumor in female RT was MG fibroadenomas, with an incidence of 80 to 90% [20, 52, 57, 85]. Other than fibroadenomas malignant tumors such as adenocarcinomas were reported in the MG tumor [20, 54, 59, 72, 86]. No studies of companion animal RTs discuss non-neoplastic lesions.

MG tumors were most often localized to the inguinal area; however, studies mention that in RTs these masses grow significantly larger than other SEM species [20]. Some masses were reported to grow from the neck to around the tail base [20, 52, 72]. Other reported CSs of a MG tumor in RTs include ulceration, secondary infection, possible mobility problems, and reproductive tract abnormalities, such as endometrial polyps, HP, and suppurative metritis [20, 52, 57, 72, 86].

### 1.4. Syrian Hamster Lesions

#### 1.4.1. Lesions of the Reproductive Tract

In Syrian HM, uterine tumors have been infrequently reported. Most studies compared laboratory Syrian HMs; therefore, making it difficult to directly compare the results to pet HMs. Hocker and others in 2017, discussed rodent oncology and specifically discussed Syrian HMs reproductive system lesions; lesions documented include leiomyosarcoma [54], leiomyoma [53], and adenocarcinoma [11, 20]. Ovarian tumors were discovered only in laboratory HMs [11, 20, 53] No male reproductive tumors were reported. In a study done by McInnes and others in 2015, non-neoplastic lesions reported were endometrial HP, granular cell HP, periarteritis, hydrometra, and endometrial cysts [84].

Possible systemic CSs seen in uterine tumors in Syrian HMs included lethargy, anorexia, abdominal distention, and vaginal discharge [20, 54].

## 2. Aim

This study aims to increase the information output of histopathological results and CSs of different lesions found on SEMs presented in the University of Veterinary Medicine, Budapest exotic clinic.

## 3. Materials & Methods

All twenty-eight samples were surgically removed and submitted within four months at the University of Veterinary Medicine, Budapest exotic clinic. Nine-teen from GPs, three from

RBs, five from RTs, and one from a Syrian HM. Of the twenty-eight samples thirteen originated from the reproductive tract. Of the thirteen reproductive tract samples, twelve were uterus samples. An ovariohysterectomy was done to remove the entire organ. One sample originated from the testicle. Castration was completed for the removal of the testicle. Of the remaining Fifteen samples, seven suspicious SC samples were surgically excised. The remaining MG samples (n=7) and miscellaneous samples (n=2) were also surgically excised. The animals were routinely premedicated with different combinations of buprenorphine, midazolam, and ketamine. Depending on the animal and procedure completed. For induction and maintenance, 2-5% V/V% Isoflurane anesthetic was used in combination with 95-98% oxygen. The animals received 9 mg/mL sodium chloride (Salsol) and a Vitamin B complex, electrolyte, amino acid, and dextrose blend (Duphlyte) infusion during the procedure. The post-operation medication consisted of an NSAID and antibiotic, such as meloxicam and trimethoprim in combination with sulfamethoxazole, respectively.

For each SC procedure, a bay leaf incision was completed with suturing. The uterus removal was a median laparotomy, an ovariohysterectomy, and finalized with layered suture closure. Once removed, the sample was placed into 8% neutral buffered formalin and left at room temperature for 24 hours, dehydrated in ethanol and xylene, embedded in paraffin, and then trimmed for slide preparation [79]. Hematoxylin and eosin (HE) staining was used on 3-4 um thick sections and reviewed under the light microscope [79].

Uterus thickening, lumen fluid, and ovarian cysts were confirmed with ultrasonography. Systemic CSs were evaluated using visual signs of lethargy, loss of appetite, and measured weight loss.

## 4. Results

### 4.1. General

Twenty-eight samples were received for histopathological examination. The samples were submitted based on suspicious changes to different tissues. To find the incidence of lesions, the average monthly visitations for each species were compared to the average monthly detection of lesions during the four-month collection period. For reference, in the previous year 389 GPs, 215 RBs, 30 RTs, and 40 HM visited the clinic. This revealed that RTs had the highest incidence of lesions per month with 50%, followed by 14.6% for GPs, 7.6% for HMs, and 4.2% for RBs (Fig. 1). Sixty-eight percent (n=19) of the samples originated from GPs, 11% (n=3) from RBs, 18% (n=5) from RTs, and 4% (n=1) from a HM. Of the twenty-eight samples, 46% (n=13) originated from the reproductive tract, 25% (n=7) from the SC tissue, 21% (n=6) from the MG tissue, 4% (n=1) from bone, and 4% (n=1) from the urinary bladder (UB).

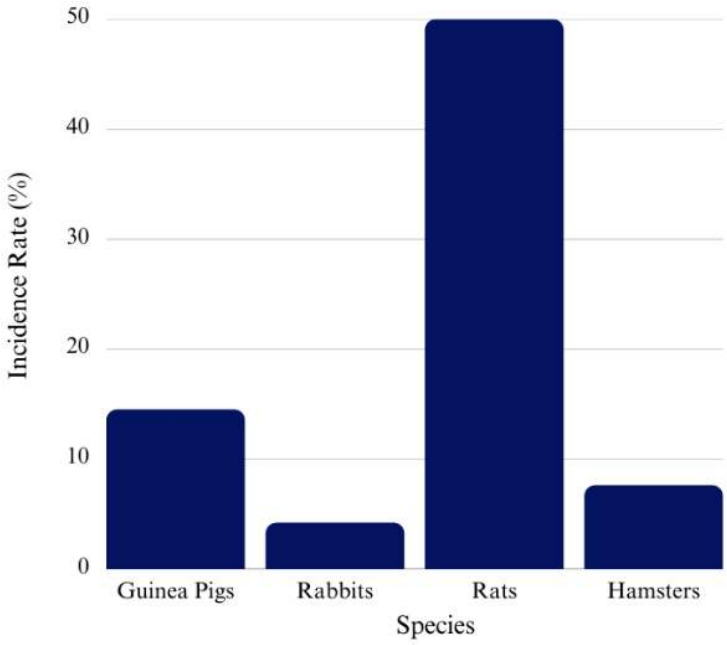


**Figure 1.** Average Lesion Incidence of Species, based on Visitation to The University of Veterinary Medicine, Budapest Exotics Clinic

### 4.2. Guinea Pigs

#### 4.2.1. Reproductive Tract Histopathological Results

Of the nineteen samples from GPs, 53% (n=10) of the samples originated from the reproductive system, specifically from the uterus. All ten samples were exclusively from intact females. The mean age affected was 4.7 years (age range 2.3 years - 6.5 years). The median age was 4.8 years. In all cases, the affected organ was completely removed.

Two of the ten samples were neoplastic changes. The remaining eight were non-neoplastic alterations of the uterus.

The two neoplastic changes from the uterus were malignant fibrosarcoma (fig. 2B), but additionally showed signs of HP. The mean age affected by fibrosarcoma was 4.8 years. On histopathological examination, one of the fibrosarcoma diagnoses additionally showed signs of regressive and vascularized changes. Three of the ten neoplastic histopathological samples showed signs of positive eosin stain uptake, one was a malignant sample.

The eight non-neoplastic alterations of the uterus consisted of six diagnoses of epithelial cell HP of the uterine glands (fig. 2A). Two of the hyperplastic findings additionally had cyst-like changes. One HP lesion only showed signs of a cyst-like enlargement of the uterine glands; while the remaining one was a follicular cyst localized in the ovary, but the uterus's result did not show any pathological changes. Two of the three non-neoplastic samples showed signs of eosin-positive stain uptake.

Of the samples collected from GP uteruses, all the animals had CSs. Three of the ten GPs presented with signs of metritis. Two of them had malignant fibrosarcoma and had lost significant weight. Each GP had at least one palpable ovarian cyst. Three of those cysts were single-sided cysts, two were found coinciding with a malignant neoplasm, and the remaining one was with HP. The remaining seven cysts were two-sided, which exclusively coincided with non-neoplastic lesions. An additional CS presented on examination was hyperkeratotic teats. 40% (n=4) GPs had signs of hyperkeratotic teats, none coincided with fibrosarcoma. All four of the hyperkeratotic teat GPs histopathology results were HP. One HP-diagnosed GP showed signs of symmetrical fur loss. Only one GP showed signs of overall weakness. It was the one GP with only ovarian cysts and no signs of uterus change.

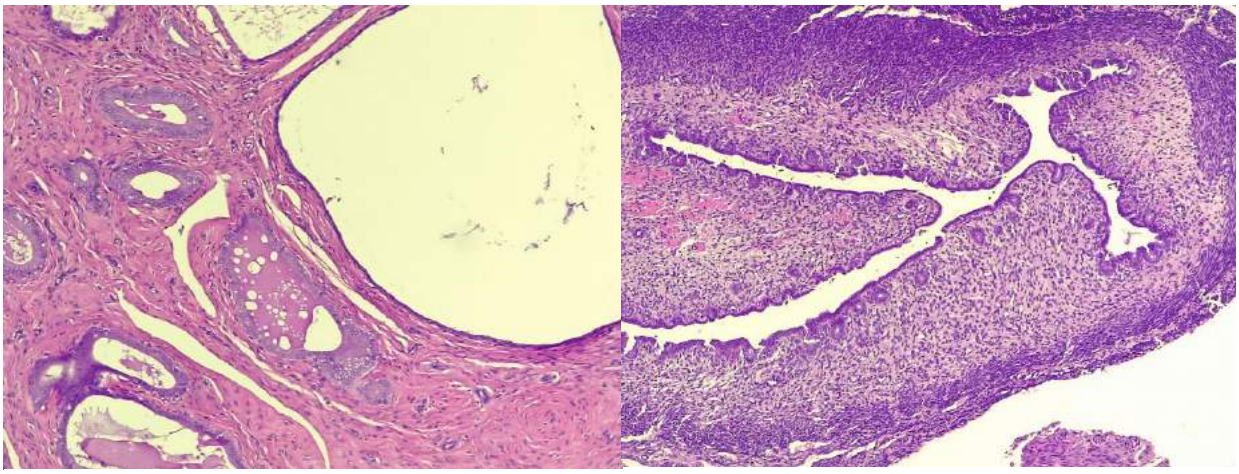

**Figure 2.** (A) Uterine Hyperplasia. (B) Fibrosarcoma.

#### 4.2.2. Cutaneous and Subcutaneous Histopathological Results

Three samples from GPs originated from the SC or cutaneous tissue. MG tissue was excluded from this section and is discussed in the following section. One sample was an intact male GP and the remaining two were intact females. The mean age submitted for histopathological review was 4.8 years (range 2.5 – 6.3). The intact male GP's result was a lipoma. The intact females' results were fibroma and the other carcinoma. All SC and cutaneous tissue reviewed by histopathology came back neoplastic. Two of the three results were benign growths. The single carcinoma histopathological description was a malignant hepatoid cell-like carcinoma. Additionally, the stroma of the tumor had minimal and medium mitotic activity. Defining the malignancy of the tumor.

All SC and cutaneous samples presented as externally palpable masses. Each mass was located at different areas of the body. The fibroma was located ventrally on the right side of the GP below the abdominal muscle, the carcinoma was on the left side below the skin, and the lipoma was discovered on the left side of the chest near the ribs. In addition to the lipoma, a similar mass was located ventrally on the chest. On examination, the carcinoma was easily movable. The fibroma had a filled and hard consistency. The GP with the fibroma was the only one to additionally have hormonal signs such as a thickened uterus and two-sided cystic ovaries. No other CSs were taken note of by the owner or veterinarian at the time of presentation.

#### 4.2.3. Mammary Tissue Histopathological Results

Of the GP lesions, 21% (n=4) originated from the MG tissue. Three of the GPs were males, and one was an intact female. All males were intact, except for one which was indefinite.

The mean age was 3.25 years (age range: 3-3.5). All the samples were neoplastic growths. Three were benign lipomas (fig. 3) and one was diagnosed as a high-grade carcinoma (Fig. 4). Additional findings on histopathological review were hyperkeratotic skin on top of a lipoma and bleeding under the mucous membrane between the glands of another lipoma.

The MG samples were all discovered by externally palpable masses located in or around the MG and were considered a potential threat to the animal and therefore, were removed and submitted for histopathology. Two of the tumors' exact locations were not noted, including the malignant tumor. One lipoma was located on both teats and the other lipoma tumors were located on the right teat. One GP with a lipoma result coincided with different hormonal CSs such as hyperkeratotic teats and a one-sided cyst. Three MG tumors showed no other CSs other than the palpable mass.

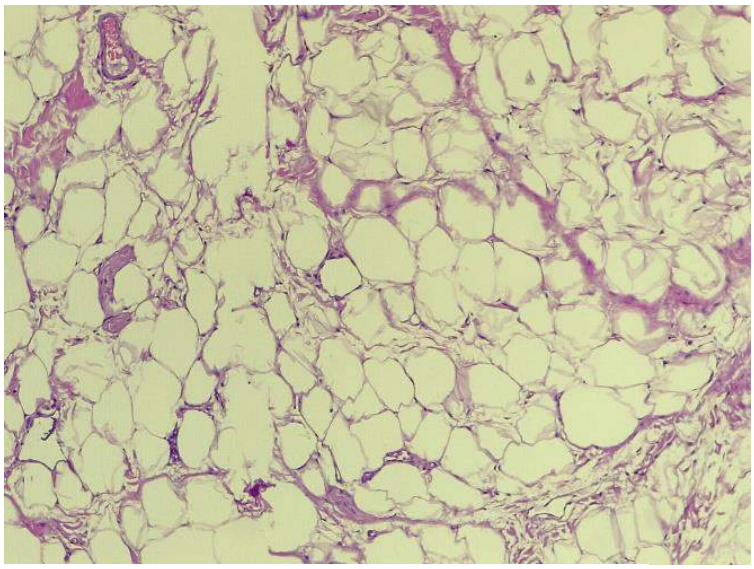

**Figure 3.** Lipoma

#### 4.2.4. Miscellaneous Histopathology Results

Of the four SEMs in this study, only GPs had other organ systems that were suspicious and sent for histopathology examination. One sample originated from the UB and one from bone. The two samples individually make up 5% of GP samples. Both samples' results were malignant neoplasms. The bone mass was diagnosed as chondrosarcoma and the UB mass as fibrosarcoma (fig. 2B). Fibrosarcoma makes up 16% of the total GP results.

Both samples were biopsied and sent for histopathological review because of suspicious mass lesions. The chondrosarcoma GP was 4.5 years of age and the GP with the fibrosarcoma was 6.8 years old. Both masses were palpable growth in different locations. The bone tumor was located on the left side of the mandible. The fibrosarcoma was located

on the UB. The chondrosarcoma GP lost its appetite and showed signs of general weakness and both GPs had lost weight. The fibrosarcoma GP also had smaller stools.

### 4.3. Rabbits

Eleven percent (n=3) of the samples were biopsied from RBs. Two of the samples originated from the reproductive tract and one from the MG tissue.

#### 4.3.1. Reproductive Tract Histopathology Results

Thirteen percent (n=2) of the total reproductive tract samples originated from RBs. The mean age affecting the reproductive tract in RBs is 1.35 years (age range 1.3-1.4) In this study, both sexes were equally affected. The histopathology result of the male was atrophy of the testicle, and the intact female had an infantile uterus. Neither of the samples were neoplastic. Of the two samples biopsied, neither of the RBs showed any CSs.

#### 4.3.2. Mammary Tissue Histopathological Result

One spayed female RB had a lesion biopsied from a MG mass. The histopathological result was a high-grade carcinoma (fig. 4.), which was the only malignant neoplasia diagnosed in an RB from this study. The RB was 4.5 years old.

The only CS found was a pea-sized lump palpated and movable in the MG area. No systemic CSs were noted at the time of examination.

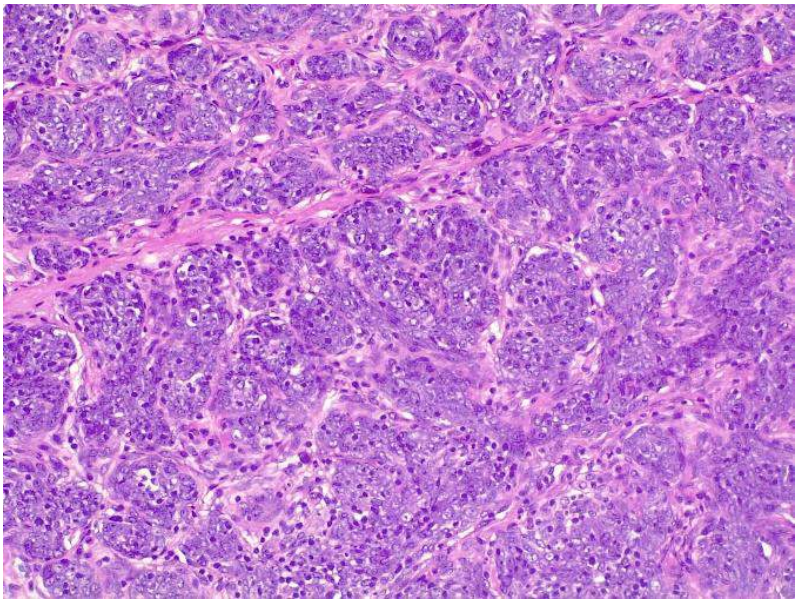

**Figure 4.** High-grade Carcinoma.

### 4.4. Rats

Eighteen percent (n=5) of the samples were biopsied from RTs for histopathological review. Two originated from the SC and cutaneous tissue. The remaining three were discovered near or in the MG tissue. No reproductive tract samples were submitted.

#### 4.4.1. Cutaneous and Subcutaneous Histopathological Results

Both samples were biopsied from intact females. The mean age affected was 1.9 years (age range: 1.8- 2 years). One sample diagnosis was fibroma (fig. 5). Histopathology showed low mitotic activity, inferring it is benign. The second sample was a malignant carcinoma.
On clinical presentation, both findings were externally palpable masses felt at different locations of the body. The rat with the fibroma diagnosis had a mass growing near the rectal and vaginal opening. The carcinoma was located on the right side of the animal. On palpation, the carcinoma was easily movable, while the fibroma had a filled consistency. Otherwise, both animals had no other CSs at the time of presentation.

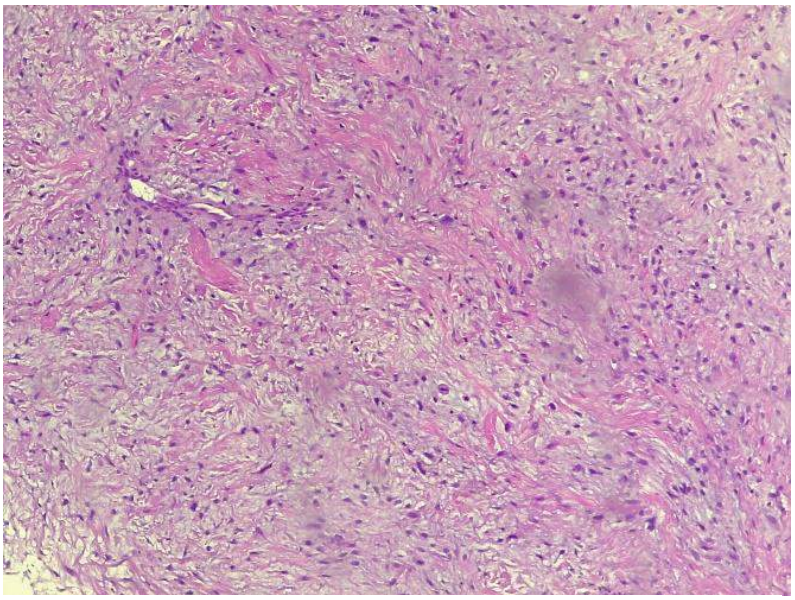

**Figure 5.** Fibroma

#### 4.4.2. Mammary Gland Histopathological Results

The remaining three RT samples originated from the MG tissue. This made up 37.5% of MG lesions biopsied from all species. All samples biopsied from RTs came from intact females. The mean age of the RTs was 2.3 years (age range 1.8 – 3 years). Two of the samples were non-neoplastic HP in the epithelial cells of the MG acinus and one finding

was a carcinoma. Histopathology of the carcinoma sample showed tumor cells with large nuclei, medium mitotic activity, and high heterogenicity, referring to a higher malignancy. Each was in one of the MGs. Two of the samples were easily movable: the carcinoma and a hyperplastic lesion. None of the RTs showed any relevant CSs.

### 4.5. Syrian Hamster

Four percent (n=1) of samples submitted originated from a pet Syrian HM. The sample was taken from the reproductive tract. Overall, makes up 7.69% of all reproductive tract samples.

#### 4.5.1. Reproductive Tract Histopathology Results

The HM was 2.8 years old, intact female. The sample from the HM was HP in the epithelial cells of the uterine glands. Histopathology showed inflammation and perivascular inflammatory cell infiltration.

The HM showed different hormonal signs such as fluid in the uterus, thickened uterus wall, long-lasting heat, and perianal discharge. In addition, the HM showed signs of bleeding in the fat tissue of the uterus and altered echogenicity of the kidney.

## 5. Discussion

### 5.1. Guinea Pigs

GPs, in the present study, were disproportionately represented. Most of the samples originated from GPs. This may be due to the rise in GPs as pets; [29, 83]. However, the Veterinarian who biopsied the samples predominately treats GPs; therefore, something to consider is that a bias exists in favor of GP patients. Based on the clinic's previous visitations, GPs had the second highest incidence of lesions in comparison to the other species with 14.6 %. No previous studies mention the incidence in comparison to other species or to a single species.

This study revealed that mid to older aged (age range 2.3 to 6.5 years old) intact female GPs were most likely to be affected by reproductive tract lesions with a mean age of 4.7 years old. Past studies also report mid to older ages affected [28, 30, 31], but that ovarian cysts could be seen in younger ages [25]. No male GPs were submitted for reproductive tract lesions in this study, which previous studies found to be rare [69, 82, 83]. The predominant organ sampled in this study was the reproductive tract of female GPs, more specifically the uterus. This finding was consistent with previous studies [26 – 30, 32, 33, 73, 77, 78]. In the present study, malignant uterine fibrosarcoma in female GPs was the most common neoplasm diagnosed; in contrast to other studies that reported that benign uterine

leiomyomas made up most of the findings [20, 27- 30]. Uterine fibrosarcoma has rarely been reported and located in one previous study by Laik-Schandelmeier and others in 2017 [27]. The reason for the different results between the studies could not be determined but is likely due to the different animal populations. Non-neoplastic lesions, however, were the most frequently diagnosed, in previous studies and this study [18, 27, 29]. The most diagnosed uterine and overall reproductive GP lesion was HP proliferations in the epithelial cells of the uterus gland. In previous studies, cysts frequently coincided with HP [31], while in this study cysts were not always coinciding with the HP. However, based on this study and previous ones if uterine thickening is noticed, HP is a possible cause.

Based on this study's findings and previous studies, the most frequent reproductive tract disorder in GPs is ovarian cysts [18, 20, 25, 28- 30, 32, 33, 70, 73, 74]. Since it was present in all the GPs, it does not help indicate whether a uterine lesion may be neoplastic or non-neoplastic. Previous studies also found ovarian cysts to frequently occur simultaneously with uterine HP and uterine neoplasia [18, 29, 30]. The believed explanation for this correlation is hormonal stimulation [29, 76]. Two theories exist either the ovarian cysts and uterine disorders are caused by a hormonal stimulation [76], or the ovarian cysts cause the hormonal imbalance inducing uterine disease [77]. In addition, in the present study, unilateral cysts were more frequently coinciding with neoplastic lesions than with bilateral ovarian cysts, which previously have not been mentioned. One study found a neoplastic change with bilateral cysts [70]. Based on the contrasting information, no correlation can be made between uni- or bilateral cysts and neoplasia. In other studies, it was only noted that both uni- and bilateral cysts exist with conflicting information about whether left or right-sided cysts are more common [73, 74].

GPs diagnosed with fibrosarcoma showed no signs of general weakness; however, weight loss and metritis were recorded. Since the predominate lesion recorded in the uterus was non-neoplastic, the CSs recorded – hyperkeratotic teats, uterine lumen, fluid in the uterus, uterine thickening, and cystic ovaries – were also likely due to a disruption of hormones. Therefore, if such CSs are noticed in an intact female GP, a hormonal process shall be considered. Although the hormonal signs were not always indicators of malignant processes, it is still best to remove the affected organ via ovariohysterectomy to avoid further hormonal symptoms and avoid potential uterine neoplasia. Especially, since similar CSs were noticed with uterine neoplasm as an ovarian cyst. The hormonal disorder could mask the neoplastic concern. If the veterinarian feels uncomfortable performing ovariohysterectomy in GPs, GnRH treatments are available [33]. The two medications that could potentially be used are

Lupron and Deslorelin, both are GnRH agonists but are currently unproven to help with ovarian cysts in GPs [33, 78].

The second most affected tissue in GPs was the MG tissue followed closely by the SC and cutaneous tissue. This conflicted with a previous study, which reported that the most common externally palpable masses on GPs were SC and cutaneous masses [24]. This difference is most likely due to the different animal populations. Both externally palpable lesions affected mid to older-aged GPs in previous studies and the present study [3, 18, 19, 24]. In the SC and cutaneous tissue, benign lesions were the most common in this study and previous [3, 18, 19, 21, 34]. In the MG, all samples were neoplastic, but only one was malignant. In this study, the most frequent diagnosis was a lipoma. No notable local or systemic clinical findings were made with either malignant or benign proliferation in the MG and SC and cutaneous tissue. Therefore, it is recommended to complete an excisional biopsy of the mass if the animal is bothered by the growth and to avoid possible tumor development.

GPs were the only species to have lesions in other parts of the body other than the reproductive tract, SC and cutaneous tissue, and MG tissue. The additional lesions were in the bone and the UB, and both were malignant lesions. Both neoplasms have been recorded in previous studies but were rare [79, 80]. The GP with chondrosarcoma showed significant CS such as loss of appetite, weight loss, and lethargy. This was the only GP with a malignant neoplasm to show obvious signs of lethargy. While the other malignant lesions only have weight loss. The GPs with fibrosarcoma in the UB like other malignant neoplasms diagnosed in GPs showed no prominent CS and were in good overall condition at the time of biopsy.

### 5.2. Rabbits

From the present study, RBs had the third most submitted number of samples, but the lowest incidence in the clinic. Similarly, to GPs in this study and previous studies, the reproductive tract was the most frequently sampled in RBs [36]. However, unlike previous claims, females and males were equally affected, all RBs affected were young, and only non-neoplastic processes were diagnosed in the reproductive tract. The lack of agreement is likely due to the small sample of RBs in this study. However, it does give us information that other disease processes and lesions are possible and should be considered when alteration is seen in the reproductive organs in RBs and shall be considered as differential diagnoses. The findings included an infantile uterus and an atrophied testicle. Suzuki and others in 2011, reported atrophy in a RB's testicle due to senile changes [59]. This RB, however, was only

1.4 years- old, therefore, this is not the case. Other previously reported reasons for testicular tissue atrophy include testicular torsion [65], and neoplastic mass [64-66]. Since the incidence of an atrophied testicle can coincide with other potential pathological processes, further examinations should be completed to rule out other complications. No other previous studies have reported an infantile uterus in RBs. The animal with the infantile uterus acted immature for its age; but other than that, neither animal presented with any coinciding systemic CS other than a noticeable morphological change to the organs.

The MG lesion identified was a malignant carcinoma, which agreed with Baum and others' 2015 study. It claimed that a high percentage of MG tumors in RBs were frequently malignant carcinomas [15]. For this reason, surgical excision with proper margins is recommended. Some studies believe there is a hormonal influence on MG tumors [16, 22]. Although they were more frequent in already spayed RBs, this is most likely due to late castration. Therefore, early castration is recommended before hormonal changes have taken place to avoid the development of MG tumors.

The RB presented with no CS other than an easily movable palpable lump.

### 5.3. Rats

RTs were documented to be prone to bumps and lumps. In this study, RTs had the highest incidence of lesions and the second most submitted samples. In contrast to these findings, not many past studies exist discussing potential pet RT lesions since most reports posted were from laboratory RTs [20]; therefore, it is difficult to apply many results to a clinical setting. All the tissue sampled from s came from externally palpable masses. In this study, external masses were predominately MG tissue lesions. MG lesions in this study affected slightly older RTs than SC and cutaneous tissue lesions, which was a similar finding in past studies [3]. Overall, externally palpable mass lesions were predominately diagnosed as non-neoplastic hyperplastic changes in the MG and the SC and cutaneous tissue neoplastic changes with a 50% chance of malignancy. Since no studies were found comparing non-neoplastic lesions, it is uncertain how these results compare to past studies. However, the present study's results did not agree with multiple previous claims. For example, the most frequent lesions are neoplastic, MG lesions are mostly fibroadenoma [20, 52, 57, 85], and in the SC and cutaneous tissue either squamous cell carcinoma [71] or soft tissue sarcoma [3] are the diagnoses. The reason for the difference in results is most likely due to the different animal populations.

No noticeable trends were seen with movability and neoplastic or non-neoplastic. No systemic signs were reported for either neoplastic or non-neoplastic lesions of the MG tissue. Further testing is recommended or an excisional biopsy to rule out malignant lesions.

### 5.4. Syrian Hamster

Based on the present samples' HMs were a low candidate for potential disease processes in tissues since only one sample was submitted for histopathological review but had a higher incidence at the sampled veterinary clinic than RBs. Not many owners may be willing to bring in their pet HMs for treatment because of the price and known life span. The HM was a senior female, The lesion was an inflammatory process of the uterus. In past studies, no such inflammatory lesions were recorded in pet Syrian HMs.

HM, like GPs showed hormonal CS. Additionally, the HM had an altered echogenicity of the kidney.

### 5.5. Disclaimer

The present study was a small sample taken from a short period of mostly clients at the University of Veterinary Medicine of Budapest. To have a more wide and accurate view of potential trends in diseases in small animals, an extended period could be used for a larger sample size. In addition to using weight loss and lethargy as systemic CSs, parameters such as body temperature, heart rate, respiratory rate, and blood results could have been included to check for additional indicator signs of disease.

**Table 1.** The species, Histopathological results, and systemic clinical signs based on the organ systems affected.

| Organ System | Species | Histopathology | CS |
|---|---|---|---|
| Reproductive Tract | | | |
| | GP | HP | Y |
| | GP | HP | N |
| | GP | HP | Y |
| | GP | HP | N |
| | GP | HP | N |
| | GP | HP and Cystic | N |
| | GP | Cystic | Y |
| | GP | Fibrosarcoma | Y |
| | GP | Fibrosarcoma | Y |
| | GP | No Lesion | N |
| | RB | Infantile Uterus | N |
| | RB | Atrophied Testicle | N |
| | HM | HP | N |
| Subcutaneous and Cutaneous Tissue | | | |
| | GP | Fibroma | N |
| | GP | Hepatoid Carcinoma | N |
| | GP | Lipoma | N |
| | RT | Fibroma | N |
| | RT | Carcinoma | N |
| Mammary Gland Tissue | | | |
| | GP | Lipoma | N |
| | GP | Lipoma | N |
| | GP | Lipoma | N |
| | GP | Carcinoma | N |
| | RT | HP | N |
| | RT | HP | N |
| | RT | Carcinoma | N |
| | RB | Carcinoma | N |
| Bone | | | |
| | GP | Chondrosarcoma | Y |
| Urinary Bladder | | | |
| | GP | Fibrosarcoma | N |

Y, yes; N, no

## 6. Conclusion

In conclusion, SEMs are popular pets and becoming more frequent patients at veterinary clinics. Therefore, knowledge of potential SEM diseases is important for every veterinarian. The goal of this study is to compare the histopathological results of SEM pet lesions and their CSs. In hopes of giving clinicians more knowledge and confidence about potential diseases in such animals. The animals with the highest incidence of lesions at the University of Veterinary Medicine, Budapest exotic clinic were RTs, and the least were RBs. Additionally, this report found that SEM lesions were 53% neoplastic of which 60% were malignant. The major concerning non-neoplastic histopathological finding was hyperplastic tissue proliferation in GPs along with cystic ovaries. Other non-neoplastic findings recorded were HP with cystic changes, atrophy, infantile organ, and no lesion discovered. All with

equal and lower likelihood. Based on this finding, it is essential to remove all potentially threatening lesions. All reproductive tract neoplasm diagnoses were made from GP samples. In the SC and cutaneous tissues, most findings were benign neoplasia and were equally from RTS and GPS. Concerning MG tissue, malignant and benign proliferations had equal probability; and GPS, RBS, and RTS were equally affected by malignant neoplasm in MG tissue. Different tissue lesions were only reported in GPs, both of which were malignant neoplasms. Based on this finding, can conclude that GPs were more prone to varying tissue location neoplasms than the other animals present in this study. An additional finding is that HMs were the least frequent visitors to veterinary clinics due to their low visitation at the clinic and the low population sampled. Although most alterations were neoplastic and most neoplastic changes were malignant, an insignificant percentage of neoplastic proliferations coincided with systemic CSs (Table 1). In summary, systemic CSs were an insignificant diagnostic tool for veterinarians treating SEMs. In addition, systemic CSs did not show a significant correlation with non-neoplastic and neoplastic changes other than weight loss, which was more prominent with neoplastic changes. Therefore, weighting of SEMs is recommended to catch potential neoplastic processes, but also catch other diseases early. Weekly weighting is recommended to owners to catch gradual or rapid weight loss and is recommended at each veterinary examination.

## 7. Abstract

Small exotic mammals are gaining popularity as household pets, and, similarly to dogs and cats, species specific diseases affect them; however, significantly fewer comprehensive epidemiological studies have been done on small exotic mammals. The aim of the present study is to compare the biopsy results of small exotic mammal pets to their clinical signs at the time of presentation. Twenty-eight samples were biopsied for histopathological review from patients at the University of Veterinary Medicine, Budapest Exotic Veterinary Clinic. The samples were examined over a four-month period. Nineteen samples originated from guinea pigs, three from rabbits, five from rats, and one sample from a Syrian hamster. Different neoplastic and non-neoplastic processes were diagnosed based on routine histopathology. To calculate the incidence of lesions, the average monthly visitations for each species were compared to the average monthly detection of lesions during the four-month collection period. This revealed that rats had the highest incidence of lesions per month with 50%, followed by 14.6% for guinea pigs, 7.6% for hamsters, and 4.2% for rabbits. Guinea pigs had the most organ systems affected (n=5), followed by rabbits and rats

(n=2), and then the hamster (n=1). In guinea pigs, most lesions originated from the uterus (52.6%). In general, the reproductive tract was the most affected organ (46.4%) with uterine lesions being predominately non-neoplastic, constituting hyperplastic proliferations (58.3%) and always coinciding with cystic ovaries. But neoplastic alterations made up 53% of all small exotic mammals' lesions reviewed and of those 60% were malignant. Carcinomas were proven to have the highest incidence regarding malignant neoplasms (56%), most frequently located in the mammary tissue (60%). In the study, systemic clinical signs were generally absent and only 21.4% of the animals showed prominent systemic signs. It is important for all general practitioner veterinarians to have proper knowledge and confidence to clinically examine and diagnose such animals. These results give veterinary clinicians useful information on possible diseases and processes of small exotic mammals.

## 8. ÖSSEFOGLALÓ

Az egzotikus kisemlősök egyre népszerűbbek házi kedvencként; és a kutyákhoz és macskákhoz hasonlóan fajspecifikus betegségek is érintik őket. Azonban lényegesen kevesebb átfogó epidemiológiai vizsgálatot végeznek egzotikus emlősökön. Jelen tanulmány célja a kistestű egzotikus emlősállatok szövettani eredményeinek összehasonlítása klinikai tünetekkel. A Budapesti Állatorvostudományi Egyetem Egzotikus Klinikáján huszonnyolc mintát vettünk kórszövettani vizsgálat céljából. A mintákat négy hónapon keresztül gyűjtöttük és dolgoztuk fel. Tizenkilenc minta tengerimalacból, három nyúlból, öt patkányból és egy szíriai aranyhörcsögből származik. A rutin kórszövettani vizsgálat alapján különböző daganatos és nem daganatos folyamatokat diagnosztizáltunk. Az egyes fajok elváltozásainak előfordulási gyakoriságainak kiszámításához az átlagos havi látogatásokat vettük, és összehasonlítottuk a négy hónapos gyűjtési időszak alatti elváltozások átlagos havi észlelésével. Ez megmutatta, hogy a patkányoknál a legmagasabb a havi elváltozások gyakorisága, 50%-kal, ezt követi a tengerimalacok 14,6%-a, a hörcsögök esetében 7,6%, a nyulak esetében pedig 4,2%. A legtöbb szervrendszeri érintettséget a tengerimalacok mutatták (n=5), ezt követték a nyulak és a patkányok kettővel, a hörcsög eggyel. Tengerimalacoknál a legtöbb elváltozás a méhből származott (52,6%). Általában a reproduktív traktus volt a leginkább érintett szervrendszer (46,4%), a méh elváltozásai túlnyomórészt nem daganatosak voltak, hiperplasztikus proliferációt (58,3%) találtunk nagy számban, szinte mindig petefészekciszták kíséretében. A neoplasztikus elváltozások pedig az összes vizsgált egzotikus kisemlős elváltozások 53%-át tették ki, és ezek 60%-a rosszindulatú volt. A rosszindulatú daganatok esetében a karcinómák előfordulása

bizonyítottan a legmagasabb (56%), leggyakrabban az emlőszövetben (60%). A vizsgálatban a szisztémás klinikai tünetek általában hiányoztak, és csak az állatok 21,4%-a mutatott klinikailag releváns elváltozásokat. Fontos, hogy minden állatorvos megfelelő ismeretekkel és rutinnal rendelkezzen ezen állatfajok klinikai vizsgálatához és diagnosztizálásához. A kutatásunk eredményei hasznos információkkal szolgálnak az állatorvosok számára az egzotikus kisemlősök lehetséges betegségeiről és előfordulási esélyeikről, amikről eddig kevés megalapozott adattal rendelkezünk.

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# Thesis progress report for veterinary students

Name of student: Lily Molnar

Neptun code of the student: C5ZDTG

Name and title of the supervisor: Dóra Csatári, PhD Student;

János Gál, Department Head of Exotic Animal and Wildlife Medicine

Department: Department of Exotic Animal and Wildlife Medicine

Thesis title: Comparing histopathological results of 28 biopsy samples from small exotic mammals – guinea pigs (Cavia porcellus), rabbits (Oryctolagus cuniculus), rats (Rattus norvegicus domesticus), and a hamster (Mesocricetus auratus) with presenting clinical signs

**Consultation – 1st semester**

| Timing | | | | Topic / Remarks of the supervisor | Signature of the supervisor |
|---|---|---|---|---|---|
| | year | month | day | | |
| 1. | 2021 | 12 | 21 | data collection, topic evaluation | |
| 2. | 2022 | 04 | 11 | data collection | |
| 3. | 2022 | 03 | 7 | article collection | |
| 4. | 2022 | 10 | 21 | article evaluation | |
| 5. | 2022 | 11 | 17 | data evaluation | |

**Grade achieved at the end of the first semester: ……5……(excellent)…..**

**Consultation – 2nd semester**

| Timing | | | | Topic / Remarks of the supervisor | Signature of the supervisor |
|---|---|---|---|---|---|
| | year | month | day | | |
| 1. | 2023 | 04 | 25 | clinical summary | |
| 2. | 2023 | 06 | 28 | histopathology data collection | |
| 3. | 2023 | 08 | 06 | histopathology evaluation | |

| | | | | | |
|---|---|---|---|---|---|
| 4. | 2023 | 10 | 15 | thesis correction, evaluation | |
| 5. | 2023 | 10 | 23 | thesis correction | |

**Grade achieved at the end of the second semester:** 5 (excellent)

The thesis meets the requirements of the Study and Examination Rules of the University and the Guide to Thesis Writing.

I accept the thesis and found suitable to defence,

.....
signature of the supervisor

Signature of the student: .....

Signature of the secretary of the department: .....

Date of handing the thesis in..... .....

**DECLARATION**

I hereby declare that the thesis entitled .... Comparing histopathological results of 28 biopsy samples from small exotic mammals – guinea pigs (Cavia porcellus), rabbits (Oryctolagus cuniculus), rats (Rattus norvegicus domesticus), and a hamster (Mesocricetus auratus) with presenting clinical signs.....

is identical in terms of content and formal requirements to the TDK research paper submitted in ….2023..... (year).

Date: …..11/13/23…..

Nov 13, 2023

Student name and signature