EPIDEMIOLOGY OF SKIN TUMOR ENTITIES ACCORDING TO THE NEW WHO CLASSIFICATION

IN DOGS AND CATS

Monier A. Mohamed Sharif

منير الصابر محمد الشريف

INAUGURAL-DISSERTATION

zur Erlangung des Grades eines
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Betreuer: Prof. Dr. Manfred Reinacher, Geschäftsführender Direktor des Institut für Veterinär-Pathologie der Justus-Liebig-Universität Giessen

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eingereicht von

Monier A. Mohamed Sharif
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Gutachter: Prof. Dr. Manfred Reinacher

Gutachterin: PD Dr. C. Pfarrer

Tag der Disputation: 26.06.2006

To the memory of my father

الى روح الوالد العزيز, اللهم اغفر له و ارحمه

CONTENTS

1. INTRODUCTION

Epithelial, melanocytic and mesenchymal skin neoplasms and non-neoplastic lesions are very common, in particular in dogs and cats and they are the most commonly diagnosed tumors in domestic animals, at least at our institute.

In 1974, the World Health Organization (WHO) published a text on the international histological classification of tumors of domestic animals, which followed, as far as possible, the WHO histological classifications of tumors in man.

A new or second edition of the international histological classification of skin, melanocytic and soft tissue tumors of domestic animals was published in 1998 with new entities and some new nomenclatures. For the time between 1998 and today, we did not find any statistical study that exposes all these tumors according to the new WHO classification. It is therefore the purpose of this study to apply the new WHO classification to the epidemiology of skin tumor entities in dogs and cats.

2. LITERATURE REVIEW

2.1. World Health Organization (WHO) classification of tumors of domestic animals

In 1966 the WHO convened a meeting of investigators on comparative oncology to work on the development of an international histological classification of tumors of domestic animals in parallel with the classification of human tumors (Beveridge and Sobin, 1974).

The WHO published the original histological classification of tumors of domestic animals in 1974 with the purpose of establishing a sound basis for comparative oncology by providing a widely accepted standard nomenclature of tumors of domestic animals and in order to advance veterinary pathology. This classification also contained tumors of the skin, and the authors were E. Weiss and K. Frese of the Institute of Veterinary Pathology, Justus Liebig University Giessen, Germany (Weiss and Frese, 1974)

In 1980, the first TNM* classification of tumors in domestic animals was published by the WHO, in support of the WHO histological classification of tumors of domestic animals. This classification provided a staging of the animal tumors to aid veterinary clinicians in planning treatment, to give some indication of prognosis, to assist in the evaluation of treatment results, to facilitate the exchange of information between treatment centres, and to contribute information on comparative values between man and animal (Owen, 1980).

In 1998 the WHO published the second edition of the histological classification of tumors of the skin and soft tissue in domestic animals to advance the old WHO edition, because new entities had been described over the past 24 years. Moreover, the nomenclature previously applied to some skin tumors was changed (Goldschmidt et al., 1998, Hendrick et al., 1998).

2.2. General population

The epidemiology depends first on the prevalence, incidence and distribution of the diseases as well as on the causes and risk factors in defined populations (Bomhard, 2001).

Our animal populations comprise dogs and cats and we describe the population of each type separately as follows:

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* The extent of the primary tumor (T), the condition of the regional lymph nodes (N), and the presence or absence of distant metastasis (M) (Matyas, 1982).

2.2.1. Dogs

A study carried out in Hannover, Germany, by Bomhard (2001) showed that the most common breeds of dogs were Mongrel, German shepherd, Dachshund, Poodle, Boxer, Cocker spaniel, Schnauzer (breed not further specified), Yorkshire terrier, Westhighland white terrier, Retriever, Sennenhund, Rottweiler, Dobermann, Airedale terrier and Muensterlaender in this order, from about 22 % for Mongrels down to 1 % for Muensterlaender, with other races at less than 1 %. An old study by the Institute of Veterinary Pathology in Giessen, Germany, carried out between 1950 and 1958 (Frese, 1960), showed no significant differences regarding breeds in comparison with Bomhard's results (2001).

Sex distribution in the dog population showed a frequent slight bias toward females rather than males, at rates of 56 % and 44 %, respectively. The percentages of castrated and uncastrated animals differ in the literature (Goldschmidt and Shofer, 1992, Bomhard, 2001), however, uncastrated animals always outnumber castrated animals. Frese (1960) on the other hand, describes a male preponderance over females at about 58 % and 42 %, respectively.

Regarding the basic population, we have found just a few publications (Frese, 1960, Eskens, 1983, Bomhard, 2001) which describe the age distribution in the dog population. Most animals were between 9 and 10-years-old (Eskens, 1983, Bomhard, 2001) and in another study between 6 and 8-years-old (Frese, 1960). More details about these studies are described below (see 2.4.2.1.)

2.2.2. Cats

The most common breed is the European shorthair cat (ESH cat), which contributes more than 85 % to the overall cat population, the two other frequent breeds are Persian and Siamese cats, which come to about 10% and 3 %, respectively, and the other 2 %, are rare breeds (Bomhard, 2001).

Sex distribution in cat populations showed a frequent slight bias to females rather than males, at 54.5 % and 45.5 %, (Goldschmidt and Shofer, 1992), or 53 % female and 47 % male, respectively (Bomhard, 2001). The percentages of castrated and uncastrated animals differ between various authors. For example, uncastrated animals represent the higher percentage in Bomhard's collection (2001), in contrast to the findings of Goldschmidt and Shofer with regard to their collection (1992).

Most cats were between 10 and 12-years-old, with about 15 % of the overall population (Bomhard, 2001) (table 41).

2.3. Anatomical division

The general division of skin tumors differs in the literature (Priester and McKay, 1980, Eskens, 1983, Goldschmidt et al., 1992, Bomhard, 2001). Bomhard (2001) divided them into tumors of the head, neck, limbs, chest, back, abdomen, perianal, tail, and some tumors without data regarding locations. The extremities are defined as limbs (arms and legs) (Pschyrembel, 2002).

2.4. Tumor statistic

A general classification of the skin tumors was performed by McClelland as early as 1940. Generally, about 1 % of dogs and 0.5 % of cats had one or more primary tumors, and the prevalence for malignant tumors in dogs was similar to that in cats. However, the prevalence of benign tumors in dogs was over 10 times the prevalence in cats (MacVean et al., 1978).

The incidence rate of benign and malignant neoplasms in dogs and cats were reported to be about 1077 cases per 100,000 dogs/year and 188 cases per 100,000 cats/year. Dogs have about six times as many neoplasms as cats. In dogs, 67.6 % of such neoplasms were found in the skin and connective tissue, in cats, 44.8 % were found in these sites (Goldschmidt and Shofer, 1992, Scott et al., 2001).

On the other hand, Goldschmidt and Shofer (1992) between 1985 and 1990 collected a total of 65,000 surgical pathology specimens from dogs and 13,250 from cats. The prevalence rates of skin tumors and tumor-like lesions were 45 % in dogs and 24 % in cats (Goldschmidt and Shofer, 1992).

Eskens (1983) reported that the skin tumor rates from necropsies and biopsies were different. He collected 3492 skin tumors from 9178 biopsies, which were 38.1 % of all biopsies, and 74 skin tumors from 1120 necropsies in dogs, which were 6.6 % of all necropsies.

2.4.1. Tissue of origin

Skin tumors are divided into mesenchymal, epithelial and melanocytic tumors as in the WHO classification, and some authors in their statistics use the term "tumor-like lesion" as a separate term (Goldschmidt and Shofer, 1992). Generally, neoplasms are composed of one tissue type only, but there are exceptions such as teratoma and mixed neoplasms which consist of multiple tissues (Cullen et al., 2002).

Mesenchymal tumors are more common and make up about 55 % of tumors in dogs and 46 % of tumors in cats (Willemse, 1991, Goldschmidt and Shofer, 1992). Epithelial tumors are less common than mesenchymal tumors in dogs (35 %) and cats (43 %). Melanocytic tumors are

relatively more common in dogs (4 %) than in cats (1 %) and tumor-like lesions are somewhat higher in dogs (11 %) than in cats (9 %) **(**Goldschmidt and Shofer, 1992). In another study, follicular tumors and tumor-like lesions together represent 10.4 % and 8.1 % of all skin tumors in dogs and cats, respectively (Abramo et al., 1999).

2.4.2. Prevalence of individual types of skin tumors

There have been many statistical studies about skin tumors, some of them old such as the study by Frese (1960), and others have followed the old WHO classification such as the study of Eskens (1983). Because of the differences regarding skin tumors in dogs and cats, we will describe the skin tumors of every kind of animal separately.

2.4.2.1. Tumors in dogs

From 400 canine skin und subcutaneous tumors that were classified by Frese (1960), without indication of sources (biopsy or post-mortem sections), 2.75 % (11 cases) were unclassified tumors (10 malignant and one benign tumor), the other 389 were classified as in table 41. The nomenclature used at that time dated before the first WHO classification, and followed a human tumor classification.

4507 cases out of 4544 skin tumors collected as biopsies by Eskens (1983), were classified as in table 41 and the other 0,81 % (37 cases) were impossible to classify. The nomenclature in this publication followed the first WHO classification of 1974.

Goldschmidt and Shofer (1992) had different populations for the different skin tumors, namely 10.300 epithelial and 14500 mesenchymal tumors and 3160 tumor-like lesions and an unknown number of melanocytic tumors. They described the general percentage of the skin tumors as follows: epithelial tumors 35 %, melanocytic tumors 4 %, mesenchymal tumors 50% and tumor-like lesions 11 %. The percentages of the individual types of tumor are represented in table 41. The nomenclature in this publication followed the first WHO classification of 1974 with minor modifications and additions.

47008 skin and subcutaneous tumors and tumor-like lesions collected as biopsies by Bomhard (2001) were divided into two groups, 46729 skin tumors and tumor-like lesions, including cysts and naevus, and 279 tumors, including ceruminal gland and anal sac gland tumors. These cases were collected over ten years (1988 -1997). The results are represented in table 41. The nomenclature in this publication followed the first WHO classification, with deviations in some points.

Disregarding the circumstances and just looking at the period of the previous studies (1960, 1983, 1992, 2001) we have found in three of them (Eskens 1983, Goldschmidt 1992 and

Bomhard 2001) benign histiocytoma at the top of the collections, then mast cell tumor in the second place, whereas histiocytoma was in the second place after hepatoid gland adenoma in Frese's collection (1960), and mast cell tumor was in the fourth place.

Hepatoid gland adenoma has gradually become less frequent, dropping from about 18 % (Frese, 1960) to 9 % (Eskens, 1983, Goldschmidt and Shofer, 1992) and to less than 6 % (Bomhard, 2001). In contrast, the number of fibrosarcoma cases gradually increased in these collections, with less than 4 % found by Frese (1960), about 5 % by Eskens (1983) and 8 % by Goldschmidt and Shofer (1992) and Bomhard (2001).

Squamous cell carcinoma at over 7 % was relatively frequent in Frese's study (1960), and at 2-3 % was low in the three other collections (Eskens, 1983, Goldschmidt and Shofer, 1992, Bomhard, 2001). Basal cell tumor was relatively low (2 %) in Frese's study (1960), while it ranged between 4 and 6 % in the results of Eskens (1983), Goldschmidt and Shofer (1992) and Bomhard (2001).

Lipoma cases were relatively lower (about 3 %) in the two first studies (Frese, 1960, Eskens, 1983) and relatively higher (6-8 %) in the last two (Goldschmidt and Shofer, 1992, Bomhard, 2001).

Some tumors were similar in all these studies such as the intra-cutaneous cornifying epithelioma (about 2 %), hemangioma (3-4 %) and sebaceous adenoma (4-7 %). However, other tumors, e.g. melanocytic tumors, varied between 11 % (Frese, 1960), 5.5 % (Eskens, 1983), 4 % (Goldschmidt and Shofer, 1992), and 6 % (Bomhard, 2001), and so do the other tumors (table 41).

2.4.2.1.1. Sex predilection

As is evident in table 42, hepatoid gland tumors were primarily neoplasms in males rather than females, with almost 89 % and 11 %, respectively, as was found by Frese (1960), Goldschmidt and Shofer (1992) and Bomhard (2001). This predilection has also been reported in most other publications (Weiss and Frese, 1974, Madewell and Theilen, 1987, Gross et al., 1992, Yager and Wilcock, 1994, Scott et al., 2001, Goldschmidt and Hendrick, 2002). Histiocytomas were also slightly more frequent in males (52-69 %) than in females (31-48 %), similar to melanomas, which were more frequent in males (about 50-61 %) than in females (39-50%) (Frese, 1960, Goldschmidt and Shofer, 1992, Bomhard, 2001). In contrast, leiomyomas and leiomyosarcomas were more common in females (76 %) than males (24 %) (Bomhard, 2001). Lipomas were also more common in females (68 %) than in males (32 %)

(Weiss and Frese, 1974, Goldschmidt and Shofer, 1992, Bomhard, 2001), and Fibromas also had a predilection for female animals (Scott et al., 2001).

Some tumors vary from author to author; basal cell tumors, for example, are more common in males according to Frese (1960) and Bomhard (2001), in contrast to Goldschmidt and Shofer (1992).

Most other skin tumors show no clear sex predilection in the literature (Weiss and Frese, 1974, Goldschmidt and Shofer, 1992, Bomhard, 2001).

2.4.2.1.2. Anatomical location

There are some tumors related to specific organs in the skin such as anal sac tumors in perianal site, meibomian gland tumors on the inner aspect of the eyelid, ceruminous gland tumors in the ear canal, eccrine (atrichial) tumors in the footpad, subungual keratoacanthoma and subungual squamous cell carcinoma, which arise from the nailbed epithelium of the forelimbs or hindlimbs. Moreover, hepatoid gland tumors from hepatoid glands, which are located primarily at the perianal region, on the dorsal and ventral aspect of the tail, in the parapreputial area in males, at the abdominal mammary region in females, on the posterior region of the hindlimbs, and on the midline of the back and thorax (Gross et al., 1992, Goldschmidt and Shofer, 1992, Goldschmidt et al., 1998, Goldschmidt and Hendrick, 2002).

Some skin cysts are also related to specific areas such as subungual epithelial inclusion cysts, which are located within the bone of the third phalanx, and tumor-like lesions such as pressure point comedones, which occur primarily on the elbow (Goldschmidt et al., 1998).

Some other tumors and tumor-like lesions can be present in one location more commonly than in another, and this group of tumors includes most of the skin tumors. An example of this group is the sebaceous adenoma, which is found mainly at the head (49.5 %) (Goldschmidt and Shofer, 1992). Another example is the trichoblastoma of the dog, which is located primary on the head and neck (Goldschmidt and Hendrick, 2002)

2.4.2.1.3. Breed disposition

Some skin tumors have been described as being more common in some breeds, the more common example being malignant histiocytosis, which was first discribed in a Miniature schnauzer dog (Scott et al., 1979), then was frequently reported in Bernese mountain dogs (Moore and Rosin, 1986, Ramsey et al., 1996) and has also been reported in various dog and cat breeds (Court et al., 1993, Goldschmidt and Hendrick, 2002). Nodular dermatofibrosis of the German shepherd dog is a rare breed-specific syndrome (Goldschmidt et al., 1998).

Another example is the mast cell tumor, which was found more commonly in Boxer, Pug and Boston than in other breeds (Madewell and Theilen, 1987, Goldschmidt and Shofer, 1992, Yager and Wilcock, 1994, Scott et al., 2001). Furthermore, subungual squamous cell carcinoma showed breed disposition in Giant schnauzer and Gordon setter and many other breeds (Goldschmidt and Shofer, 1992, Goldschmidt and Hendrick, 2002).

2.4.2.1.4. Age distribution

Generally, it is known that cancer essentially represents an illness of the higher age, however, it is yet to be discussed whether the frequency of the malignome continues to increase up to the highest age-groups or whether it sinks again after a highpoint in a certain age-group (Frese, 1960).

Individually, there are some tumors which are found in young animals more commonly than in old animals. The more common examples are canine cutanous histiocytoma and papilloma, the majority of which occurr in young dogs, but dogs of any age can be affected (Goldschmidt and Shofer, 1992, Goldschmidt and Hendrick, 2002). Regarding tumor-like lesions, there are also two examples, dermoid cyst and the follicular cyst, which are both more frequently found in young animals than in adults **(**Bomhard, 2001).

2.4.2.2. Tumors in cat

Goldschmidt (1992) has described different types of various skin tumors: 1400 epithelial tumors, 1550 mesenchymal tumors, 280 tumor-like lesions and an undefined number of melanocytic tumors in cats. He reports the percentage of the skin tumors as follows: mesenchymal tumors 47 %, epithelial tumors 43 %, tumor-like lesions 9 %, and melanocytic tumors 1 %. The prevalences of individual skin tumors are presented in the table 43.

12387 skin tumors, subcutaneous tumors and tumor-like lesions were mentioned by Bomhard (2001), who divided them in two groups, namely 12087 skin tumors and tumor-like lesions including cysts and naevus, and 300 tumors including ceruminal gland and anal sac gland tumors. Some tumors, as intra-cutaneous cornifying epitheliomas were mentioned by Bomhard (2001) (as in table 43), however, intra-cutaneous cornifying epitheliomas were not normally found in cats (Goldschmidt et al., 1998), but were common in dogs (Goldschmidt et al., 1998, Goldschmidt and Hendrick, 2002). Malignant histiocytomas (as in table 43) constitute 0.21 % of all the collection of Bomhard (2001), and that equals three cases.

Fibrosarcoma is the most common tumor of the skin and subcutaneous connective tissue in the cat in the greater part of the literature (Stiglmair-Herb, 1987, Joerger, 1988, Goldschmidt

and Shofer, 1992, Gross et al., 1992, Bomhard, 2001, Goldschmidt and Hendrick, 2002), however, the prevalence varies and is about 44 % in Stiglmair-Herb (1987) and Bomhard (2001) and about 17 % in Goldschmidt and Shofer (1992). This tumor has increased in prevalence over the last decade, because of its association with vaccination (Goldschmidt and Hendrick, 2002) and is more prevalent in European cats (Miller et al., 1991).

Basal cell tumor is more common in cats than in dogs (Goldschmidt and Hendrick, 2002), and it is in the second place with about 11.4 % -18.5 % of all skin tumors in the studies of Stiglmair-Herb (1987), Joerger (1988), Goldschmidt and Shofer (1992) and Bomhard (2001), and is reported as the most common skin tumor at 26.1 % by Miller et al. (1991).

Other common tumors are squamous cell carcinoma, apocrine adenoma, mast cell tumor and lipoma (Stiglmair-Herb, 1987, Joerger, 1988, Miller et al., 1991, Goldschmidt and Shofer, 1992, Bomhard, 2001).

2.4.2.2.1. Sex predilection

No tumors with a marked sex predilection have been found in cats, however, Goldschmidt and Shofer (1992) report that some tumors show a slight deviation towards one of the sexes in either species. More than 60% of basal cell tumors, sebaceous carcinomas, cutaneous malignant melanomas, malignant fibrous histiocytomas, and peripheral nerve sheath tumors were found in females. However, apocrine adenoma, trichoepithelioma, cutaneous melanoma, lipoma, cutaneous hemangiosarcoma, cutaneous lymphangioma, cutaneous mast cell tumor, ceruminous cysts were less than 49 % in females. Other tumors and tumor-like lesions ranged around the percentages of the general population, which were 54.5 % females and 45.5 % males (Goldschmidt and Shofer, 1992).

2.4.2.2.2. Anatomical location

Some tumors are related to specific organs in the skin such as anal sac tumors in perianal sites, meibomian gland tumors on the inner aspect of the eyelid, ceruminous gland tumors in the ear canal, and eccrine tumors in the footpad (Goldschmidt and Shofer, 1992, Goldschmidt et al., 1998, Goldschmidt and Hendrick, 2002). Moreover, feline vaccine-associated fibrosarcoma arise at vaccination sites on the neck, thorax, lumbar region, flank and limbs (Goldschmidt and Hendrick, 2002), and feline ventral abdominal angiosarcoma arise in ventral abdominal region (Swayne et al., 1989, Goldschmidt et al., 1998). Also, some other tumors and tumor-like lesions can occur in one location more frequently than in others, and this group of tumors includes the majority of skin tumors. As an example of this group, 57.2

% of apocrine adenomas and 50.0% of apocrine ductal adenomas have been found at the head (Goldschmidt and Shofer, 1992).

2.5. Skin tumors

The following nomenclature and classification follows, as closely as possible, the new WHO classification. An understanding of the embryogenesis of the skin is helpful in understanding this tumor nomenclature (Goldschmidt et al., 1998).

2.5.1. Epithelial and melanocytic tumors of the skin

2.5.1.1. Epithelial tumors without squamous or adnexal differentiation

2.5.1.1.1. Basal cell tumors (basal cell epithelioma)

Basal cell tumor was a benign neoplastic proliferation of cells that recapitulate the basal cell layer of the normal epidermis. In the new WHO classification system, the majority of the tumors that were previously described as a basal cell tumors in the dog and the spindle cell type of basal cell tumor in the cat has been reclassified as trichoblastoma (Goldschmidt et al., 1998, Goldschmidt and Hendrick, 2002).

A basal cell tumor, as the term is currently used, is a dermal mass composed of islands of tumor cells in a moderately fibrous stroma, and the dermal tumor have an association with the overlying epidermis. Neoplastic cells are either small and round or polyhedral, with little cytoplasm and ovoid nuclei. Most tumors show little nuclear pleomorphism and variable mitotic activity. Central cystic degeneration of the tumor lobules may be found. Melanin pigment can also be found within the cytoplasm of tumor cells. Melanophages may be present in the stroma and within the cyst center.

Basal cell tumor differs from basal cell carcinoma by the lack of invasion and the associated fibroplasia at the periphery of the benign tumors (Goldschmidt et al., 1998, Goldschmidt and Hendrick, 2002).

Historical development of basal cell tumor classification (Diagram 1 & 2)

Moulton (1961) mentioned that solid basal cell tumor was the common form and some tumors formed elongated cords and loops, but did not form lumina. Trichoepithelioma was considered a subtype of basal cell tumor and described as basal cell tumors which form structures resembling hair (Moulton, 1961). However, Sedlmeier et al. (1967) have described more clearly the histological structures and have described the pure solid, bud-like, medusoid and ribbon-like subtypes of the solid type. Other types are the adenoid, cystic and keratotic types, and they have pointed out that the mixed forms are not seldom. A clear definition of the

adenoid type is found in this study, which is described as glandular-like structures with no real lumen but connective tissues, usually with mucoid degeneration (Sedlmeier et al., 1967).

Weiss and Frese (1974) stated in the first WHO classification that there were slight differences in the arrangement of types and subtypes of the tumors compared to previous categorization. There were solid, ribbon-like, medusoid, adenoid, cystic, basosquamous varieties. Superficial multicentric, morphoea, and fibroepithelial types had been described in man, but had not been shown to occur in animals (Weiss and Frese, 1974).

Stannard and Pulley (1978) use the term basal cell epithelioma instead of basal cell tumor, and they describe the adenoid tumor type more precisely as a subtype of the ribbon type as follows: "the stroma between the strands of cells in the ribbon type frequently undergoes mucinous degeneration, giving a distinct glandular appearance to the tumor. When this is a prominent feature, the term adenoid basal cell epithelioma has been used". They summarize basal cell tumors as: solid, cystic, ribbon (adenoid), and medusoid, and they point out that mixed-form is not uncommon.

Seiler (1982) describes tumors in three dogs that resemble the granular basal cell tumor (carcinoma) of man.

Diters and Walsh (1984) describe the trabecular type in the cat under solid basal cell tumor without mentioning the term "trabecular" and describe one histological figure which appears identical with the trabicular type of basal cell tumor as follows: "solid basal cell tumor characterized by variably sized and shaped tumor masses with peripherally radiating epithelial buds".

Pulley and Stannard (1990) give a description similar to that mentioned previously (Stannard and Pulley, 1978).

Gross et al. (1992) describe trichoblastomas separately from basal cell tumors.

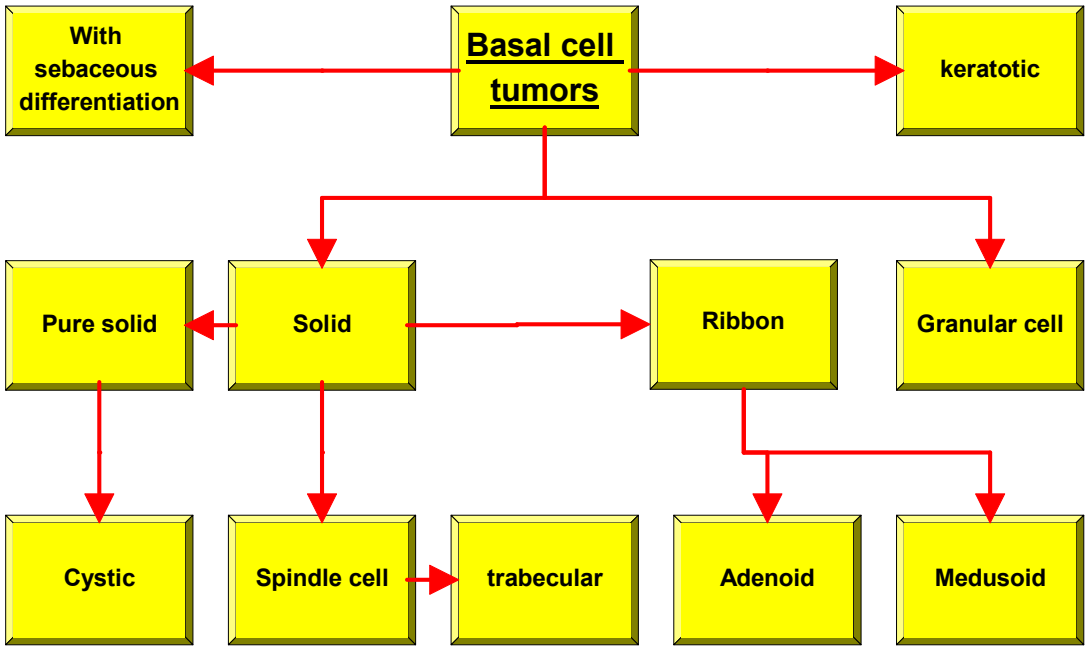
Yager and Wilcock (1994) define sebaceous epithelioma as a maturational variant of basal cell tumor.

The new international WHO histological classification of tumors of domestic animals by Goldschmidt et al. (1998) reclassifies the majority of basal cell tumors in the dog and the spindle cell type of basal cell tumor in the cat as trichoblastomas (ribbon, trabecular, granular cell and spindle cell trichoblastoma). The medusoid type is subsumed under the ribbon type, and sebaceous epithelioma under sebaceous gland tumors. Keratotic basal cell tumor is classified under tumors of the epidermis as basosquamous carcinoma.

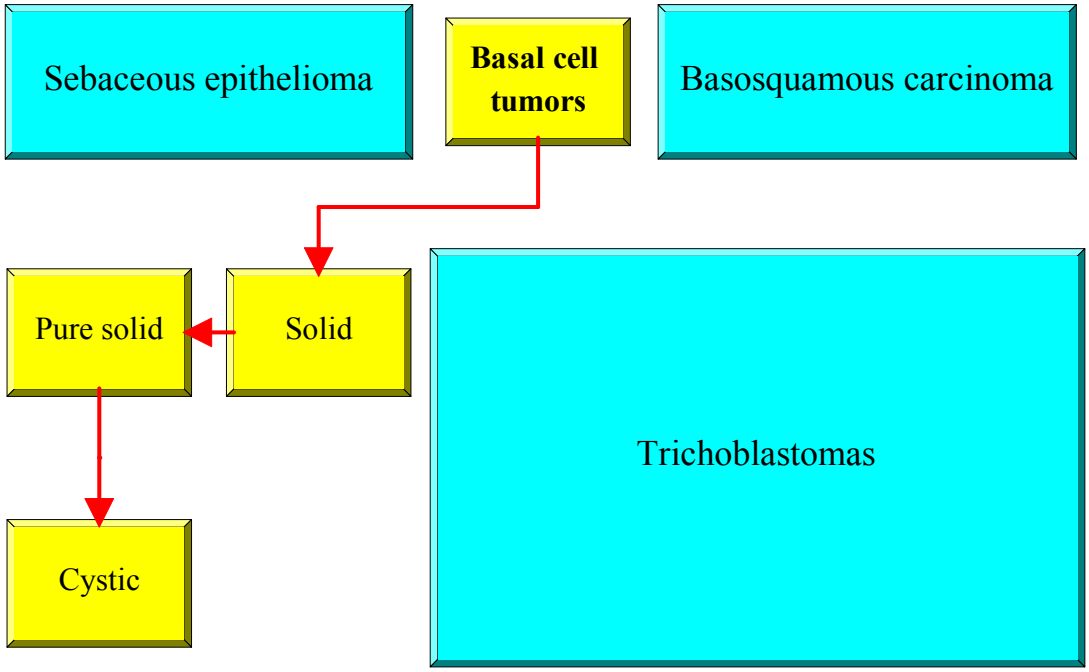
Meuten (2002), in his fourth edition, follows the new WHO classification with an additional separate medusoid type under the trichoblastoma.

In brief:

Diag. 1: Old classifications



Diag. 2: New classification



2.5.1.1.2. Basal cell carcinoma

This is a low-grade malignant proliferation of cells that recapitulate the basal cell layer of the normal epidermis or the adnexa. This neoplasm shows no differentiation of any adnexal structures and may have epidermal contiguity that can be multifocal. Histologic variants of basal cell carcinoma are infiltrative and clear cells (Goldschmidt et al., 1998).

2.5.1.1.2.1. Infiltrative basal cell tumor

These may have an association with the overlying epidermis, with cords of primitive basaloid cells extending into the dermis and occasionally into the subcutis. The tumor cells have small, hyperchromatic nuclei with scant cytoplasm, and mitotic figures may be numerous, mostly accompanied by an extensive proliferation of stromal fibroblasts. This tumor has no adnexal differentiation, a fact that allows it to be differentiated from sebaceous epithelioma and malignant trichoepithelioma (Goldschmidt et al., 1998).

2.5.1.1.2.2. Clear cell basal cell tumor

This is an uncommon and newly classified variant, in which the tumor cells are large and polygonal and have clear or finely granular cytoplasm. Its nuclei are ovoid and uniform with small nucleoli and a variable number of mitoses (Goldschmidt et al., 1998, Goldschmidt and Hendrick, 2002).

2.5.1.2. Tumors of the epidermis

This group of tumors includes papilloma (papillomatosis) and inverted papilloma as benign tumors (Campbell et al., 1988, Shimada et al., 1993). Actinic keratosis (Hargis and Thomassen, 1979), multicentric squamous cell carcinoma in situ or bowen-like disease (Baer and Helton, 1993), squamous cell carcinoma and basosquamous carcinoma represent the malignant tumors (Goldschmidt et al., 1998). Squamous cell carcinoma has two uncommon histologic variants, acantholytic and spindle cell squamous cell carcinoma (Goldschmidt et al., 1998, Goldschmidt and Hendrick, 2002). Another variant described as signet-ring squamous cell carcinoma has been reported (Espinosa et al., 2003)

The benign, virus-induced fibropapilloma of the cattle, as in the old WHO classification, is not found in the new WHO classification.

Actinic keratosis and multicentric squamous cell carcinoma in situ were not classifid in the old WHO classification and were reported in the time between the old and new classifications (Hargis and Thomassen, 1979, Gross and Brimacomb, 1986, Baer and Helton, 1993).

Basosquamous carcinoma, which was classified in the old WHO classification as a variant of basal cell tumor (Weiss and Frese, 1974), is considered an epidermal tumor in the new WHO classification (Goldschmidt et al., 1998).

2.5.1.3. Tumors with adnexal differentiation

2.5.1.3.1. Follicular tumors

This group consists of the following tumors: infundibular keratinizing acanthoma, tricholemmoma, trichoblastoma, trichoepithelioma and pilomatricoma.

Only trichoepithelioma and pilomatricoma (under the name of necrotizing and calcifying epithelioma {Malherbe}) were classified under follicular tumors in the old WHO classification (Weiss and Frese, 1974). Infundibular keratinizing acanthoma was classified separately in the old WHO classification under epithelial tumors and tumor-like lesions, and not as hair follicle tumor as it is in the new WHO classification.

Some other hair follicle tumors such as trichofolliculoma in animals have been reported as common tumors in guinea pigs and constitute 45 % of all skin tumors in these animals (Frank and Frese 1988). However, they have also been reported as rare benign neoplasms of dogs and cats (Gross et al., 1992, Scott et al., 2001). Trichofolliculoma was mentioned in the old WHO classification as a tumor of man and at that time had not yet been described in animals (Weiss and Frese, 1974), however, it is not mentioned in the new WHO classification.

2.5.1.3.1.1 Infundibular keratinizing acanthoma

This tumor is also called intra-cutaneous cornifying epithelioma (Goldschmidt et al., 1998). It was designated as keratoacanthoma in the U.S.A., however, this name was not accepted in the old WHO classification (Weiss and Frese, 1974). According to the new WHO classification, the diagnosis of keratoacanthoma should be reserved for tumors of subungual origin (Goldschmidt et al., 1998). This tumor must be differentiated from squamous cell carcinomas, trichoepitheliomas, and epidermal inclusion cysts (Stannard and Pulley, 1975). Cysts with epithelial proliferation were considered an early stage of infundibular keratinizing acanthoma in the old WHO classification (Weiss and Frese, 1974).

2.5.1.3.1.2 Tricholemmoma

This tumor has recently been classified in the new WHO classification; it is characterized by external root sheath differentiation and has two types, the inferior and the isthmic type. The first cases in dogs were reported by Diters and Goldschmidt (1983), who described the bulb or

inferior type, and by Walsh and Corapi (1986), who described the isthmic type. Some authors use the term trichilemmoma instead of tricholemmoma (Murphy and Elder, 1990).

2.5.1.3.1.3 Trichoblastoma

Trichoblastomas have mostly been reported as basal cell tumors in the literature (Sedlmeier et al., 1967, Stannard and Pulley, 1978, Madewell and Theilen, 1987, Goldschmidt and Shofer, 1992, Bomhard, 2001, Goldschmidt and Hendrick, 2002) and they are mentioned separately by Gross et al. (1992). Trichoblastoma is a new term used in the WHO classification. It has been reclassified from the majority of those tumors that were previously categorized as basal cell tumors in the dog, horse and sheep, and as spindle cell form of a basal cell tumor in the cat (Goldschmidt and Hendrick, 2002). Trabecular trichoblastoma was also categorized as a type of trichoblastoma, which is more frequent in cats (Goldschmidt et al., 1998, Goldschmidt and Hendrick, 2002) but the authors did not explain why and that this tumor is reclassified from basal cell tumor.

Trichoblastoma is a benign tumor and has different types including ribbon, trabecular, granular cell and spindle cell (Goldschmidt et al., 1998) and medusoid types (Goldschmidt and Hendrick, 2002). Some authors state that the mixed forms are not uncommon (Sedlmeier et al., 1967, Stannard and Pulley, 1978).

The ribbon, medusoid and granular cell types are mostly seen in dogs, while trabecular and spindle cell type are more frequent in cats (Goldschmidt and Hendrick, 2002).

Generally, trichoblastomas are common in dogs and cats, uncommon in horses and rare in other species (Goldschmidt and Hendrick, 2002). The granular cell type is very rare and only a few cases have been reported in dogs and rats (Seiler, 1982, Courtney, 1992, Yoshitomi and Boorman 1994). The granular cell trichoblastoma in many aspects resembles granular cell myoblastoma (Seiler, 1982), however, both tumors generally are of different origin (mesenchymal and epithelial origin), as they are classified in the new WHO classification (Goldschmidt et al., 1998, Hendrick et al., 1998). This variation may lead to histologic confusion with tumors containing areas of sebaceous cell differentiation (Seiler, 1982).

In human pathology the first description of trichoblastoma was given by Headington and French (1962). Trichoblastomas are rare skin tumors (Yu et al., 2005). Five main patterns have been described in human trichoblastomas, namely large nodular, small nodular, cribriform, racemiform, and retiform, which may be found as an exclusive pattern, but also as combinations of two or more patterns within one tumor (Ackerman et al., 1993). Many sporadic cases of other variants have been reported, namely clear cell variants, trichoblastoma

with apocrine and sebaceous differentiation (Tronnier, 2001, Usmani et al., 2002, Yu et al., 2005) and melanotrichoblastoma (Kanitakis et al., 2002). Furthermore, trichoblastic carcinomas have also been reported (Rofagha et al., 2001, Kazakov et al., 2004). Granular cell trichoblastoma is not found in the literature on human pathology, but granular cell basal cell carcinoma has been reported (Dundr et al., 2004).

Malignant variants in domestic animals are not mentioned in the new WHO classification. Only one report of follicular stem cell carcinoma with metastasis, lymphatic invasion and necrosis in a dog has been published (Mikaelian and Wong, 2003).

2.5.1.3.1.4 Trichoepithelioma

Only a benign tumor was classified in the old WHO classification, however, two dogs with malignant variants with metastases in lymph node and lung have been reported (Sells and Conroy, 1976). The malignant trichoepithelioma (matrical carcinoma) is included in the new WHO classification (Goldschmidt et al., 1998).

2.5.1.3.1.5 Pilomatricoma

It is also called pilomatrixoma or necrotizing and calcifying epithelioma of Malherbe, and this benign tumor is included in both WHO classifications (Weiss and Frese, 1974, Goldschmidt et al., 1998). An aggressive malignant tumor with metastases in bone, lung and lymph nodes has been reported (Rodriguez et al., 1995). However, the malignant variant was missing in the old WHO classification, and it is called malignant pilomatricoma or pilomatrix carcinoma in the new WHO classification (Goldschmidt et al., 1998).

2.5.1.3.2. Nailbed tumors

This is a newly classified group of tumors arising from the nailbed epithelium and it consists of one benign (Subungual keratoacanthoma) and one malignant tumor (Subungual squamous cell carcinoma) (Goldschmidt et al., 1998, Goldschmidt and Hendrick, 2002).

The old sources of subungual keratoacanthoma in animals are mentioned by Walder and Barr (1984). Subungual keratoacanthoma is an uncommon tumor and has been described only in dogs and cats (Goldschmidt and Hendrick, 2002). In humans, it is also a rare tumor and can spontaneously regress, and it must be differentiated from squamous cell carcinoma (Sinha et al., 2005). This tumor may cause lysis of the phalangeal bone in animals and humans (Goldschmidt et al., 1998, Sinha et al., 2005).

2.5.1.3.3. Sebaceous and modified sebaceous gland tumors

This group consists of three subgroups, namely sebaceous, meibomian and hepatoid tumors. They are further divided as follow: Sebaceous adenoma, sebaceous ductal adenoma, sebaceous epithelioma, sebaceous carcinoma, meibomian adenoma, meibomian ductal adenoma, meibomian epithelioma, meibomian carcinoma, hepatoid gland adenoma (perianal gland adenoma, circumanal gland adenoma), hepatoid gland epithelioma (perianal gland epithelioma, circumanal gland epithelioma) and hepatoid gland carcinoma (perianal gland carcinoma, circumanal gland carcinoma) (Goldschmidt et al., 1998).

Meibomian gland tumors were categorized in the old WHO classification under the tumors of the eye and adnexa (Kircher et al., 1974).

Hepatoid gland tumors were categorized in the old WHO classification under two organs, the skin (Weiss and Frese, 1974) and the lower alimentary tract (Head, 1976).

Among these types, there is a newly classified tumor named epithelioma, which is characterized by a preponderance of basaloid cells with low malignancy behaviour.

Sebaceous and meibomian ductal adenomas have also been newly classified and are characterized by the presence of majority of ducts (Goldschmidt et al., 1998, Goldschmidt and Hendrick, 2002).

Weiss and Frese (1974) subdivide hepatoid gland adenomas into adenomas with secondary vascularization and adenomas with transitional cell forms, which are more common. Those hepatoid gland adenomas with vascularization are characterized by large glandular areas with small vessels and islands of soft tissue surrounded by reserve cells, and their recurrence is more frequent than that of others. Goldschmidt and Hendrick (2002) describe that some hepatoid gland adenomas show extremily ectatic vessels within the interlobular stroma.

2.5.1.3.4. Apocrine and modified apocrine gland tumors

This group consists of three subgroups, apocrine, ceruminous and anal sac gland tumors, which are divided as follows: Apocrine adenoma, complex and mixed apocrine adenoma, apocrine ductal adenoma, apocrine carcinoma, complex and mixed apocrine carcinoma, apocrine ductal carcinoma, ceruminous adenoma, complex and mixed ceruminous adenoma, ceruminous gland carcinoma, complex and mixed ceruminous carcinoma, anal sac gland adenoma (adenoma of the apocrine glands of the anal sac) and anal sac gland carcinoma (carcinoma of the apocrine glands of the anal sac) (Goldschmidt et al., 1998).

Apocrine ductal adenomas were called papillary syringadenoma in the old WHO classification (Weiss and Frese, 1974).

Anal sac tumors were categorized under tumors of the lower alimentary tract in the old WHO classification (Head, 1976).

Ceruminous gland tumors are included in the new classification, but are not found in the old WHO classification.

Signet-ring-cell carcinoma is a rare tumor mentioned in the old WHO classification (Weiss and Frese, 1974), but it is not included in the new one.

Canine clear cell variant of apocrine gland adenoma has been reported (Nile et al., 2005), but is not found in either WHO classification.

Clear cell or balloon-cell sweat gland carcinoma was first reported as follicular stem cell carcinoma by Mikaelian and Wong (2003), and then has been rediagnosed as clear cell or balloon-cell sweat gland carcinoma by Walder (2005).

2.5.1.3.5. Eccrine (atrichial) tumors

This group of tumors was classified under sweat gland tumors in the old WHO classification and includes spiradenoma and adenocarcinoma (Weiss and Frese, 1974). This rare group of footpad tumors includes eccrine adenoma and eccrine carcinoma (Goldschmidt et al., 1998, Goldschmidt and Hendrick, 2002).

2.5.1.4. Tumors metastatic to the skin

In the old WHO classification, this group was also categorized under secondary tumors of the skin (Weiss and Frese, 1974). Pulmonary carcinoma with digital metastasis is the most common tumor metastatic to the skin in cats, while mammary carcinoma with cutaneous metastasis is most often seen in dogs. An implantation metastasis secondary to prior surgery of prostatic carcinoma, transitional cell carcinoma and colonic carcinoma might be found in the skin (Goldschmidt et al., 1998). Many other cases of tumors metastatic to the skin were reported for dogs such as duodenal adenocarcinoma (Juopperi et al., 2003), pharyngeal carcinomas, oral melanomas, pancreatic ductal adenocarcinoma, jejunal adenocarcinoma (Scott et al., 2001) and malignant seminomas (Spugnini et al., 2000, Takiguchi et al., 2001). Gastric carcinoma with metastasis to the skin has been found in a cat (Scott et al., 2001).

2.5.1.5. Cysts

This group is found in both WHO classifications with many differences, and is described in detail because of its significance in our work.

The classifications of skin cysts in the old and the new WHO classifications are summarized as follows:

New WHO classification	Old WHO classification
1 Infundibular cyst (epidermoid cyst, epidermal cyst, epidermal inclusion cyst). 2 Dilated pore. 3 Isthmus cyst. 4 Panfollicular (trichoepitheliomatous) cyst. 5 Dermoid cyst (dermoid sinus). 6 Sebaceous duct cyst. 7 Apocrine cyst and apocrine cystomatosis. 8 Ciliated cyst. 9 Subungual epithelial inclusion cyst.	1- Epidermal cyst. 2- Dermoid cyst. 3- Follicular cyst. 4- Cyst with epithelial proliferation.

2.5.1.5.1. Dermoid cyst

This cyst has been classified in both, the old and new WHO classification. It is also known as pilonidal cyst (Goldschmidt and Shofer, 1992) and has been defined as a congenital dermal and/or subcutaneous cyst lined by epidermis with mature dermal and appendageal structures in the cyst wall and hair and keratin in its lumen (Goldschmidt et al., 1998). It has rarely been observed in dogs and cats (Scott et al., 2001).

Dermoid sinus has also been reported as a different lesion in dogs (Cornegliani et al., 2001, Hillbertz, 2005). This lesion is also called dermoid cyst (Gross et al., 1992). However, there are anatomical differences between a dermoid sinus and a dermoid cyst. A dermoid sinus is an inherited abnormality in Rhodesian ridgeback dogs derived from a neural tube, which is an invagination of the skin, connecting it with the dura mater in the vertebral canal or to an intervening structure. It is characterized by the presence of a tuft of hair protruding from each sinus and sometimes complicated by infection with drainage (Blood and Studdert, 1999). In contrast, a dermoid cyst is a closed epithelium-lined sac or capsule containing a semi-solid or liquefied substance (Goldsmith and Shofer, 1992). Dermoid sinus has also been reported in a Golden retriever dog (Cornegliani et al., 2001), and nasal dermoid sinuses in dogs have also been frequently reported (Bailey et al., 2001, Burrow, 2004).

2.5.1.5.2. Epidermal cyst

This has been classified in both WHO classifications, and is also called infundibular, epidermoid and epidermal inclusion cyst. It is defined as a simple cyst lined by stratified squamous epithelium, and all four layers of the normal epidermis or infundibulum, including granular cell layer, are present (Goldschmidt et al., 1998). The cyst cavity contains lamellar,

often concentrally arranged keratin and, if serial sections are employed, has often been found to be connected to a rudimentary hair follicle (Scott et al., 2001). A true epidermal cyst has been found secondary to traumatic implantation of the epidermis into the dermis (Goldschmidt and Shofer, 1992). Persistent epidermal cysts may develop into squamous carcinomas (Jubb et al., 1993).

2.5.1.5.3. Follicular cyst

This cyst was categorized in the old WHO classification. It develops through the retention of follicular or glandular products (congenital or acquired), and is filled with horny cells or lamellae, hair and cholesterol crystals. Sebaceous or apocrine sweat glands or atrophic hair follicles may be seen running into the base of the cyst. The majority of cutaneous cysts in animals are follicular cysts (Weiss and Frese, 1974), and they can be further categorized by the level of the follicle from which they have developed into infundibular, isthmus, matrical, panfollicular cysts (Scott et al., 2001). The term follicular cyst is not mentioned in the new WHO classification; however, the subtypes infundibular, isthmus and panfollicular are described separately in the new WHO classification (Goldschmidt et al., 1998).

2.5.1.5.4. Apocrine cyst

This cyst was mentioned under follicular cysts in the old WHO classification (Weiss and Frese, 1974), and is classified separately in the new WHO classification. It is an intradermal cyst lined by apocrine secretory epithelium and filled with clear secretion. Multiple cysts at multiple sites are referred as apocrine cystomatosis (Goldschmidt et al., 1998) and this kind of cyst is common in dogs (Weiss and Frese, 1974).

2.5.1.5.5. Sebaceous duct cyst

This cyst has been classified under follicular cysts in the old WHO classification (Weiss and Frese, 1974). It is defined as a cyst lined by a thin squamous epithelium of the sebaceous duct and surrounded by hyperplastic sebaceous glands (Goldschmidt et al., 1998) and this kind of cyst is very rare in dogs (Weiss and Frese, 1974).

2.5.1.5.6. Matrical cyst

It derives from the matrical or inferior segment of the hair follicle and is lined by deeply basophilic, basaloid epithelial cells that abruptly keratinize, forming shadow cells. This cyst is

regarded as a variant of pilomatricoma (Gross et al., 1992), and is not found in the new WHO classification.

2.5.1.5.7. Cyst with epithelial proliferation

It is considered an early stage of intracutaneous cornifying epithelioma (Frese and Weiss, 1969), and should be classified as an infundibular keratinizing acanthomas in the new WHO classification (Weiss and Frese, 1974).

2.5.1.5.8. Cysts with precarcinomatous epithelial transformation

These are very rare in animals, and show transformation into squamous and basal cell carcinoma (Frese and Weis, 1969). Squamous cell carcinomas arisen from follicular cysts have also been reported (Scott et al., 2001). These cysts are not mentioned in either WHO classification.

2.5.1.5.9. Branchial cyst

This cyst has been found in the ventral cervical region and derives from the second branchial pouch. A thin wall lined by pseudostratified, nonciliated, columnar epithelial cells is characteristic of this cyst (Karbe and Nielsen, 1965, Clark and Kostolich, 1989, Scott et al., 2001). It is extremely rare in dogs and cats (Scott et al., 2001) and individual cases in some other animals, namely mice, cattle and horses have been reported (Smith and Gunson, 1977, Hance and Robertson, 1992, France et al., 2000). However, this cyst has not been classified in either WHO classification.

2.5.1.5.10. Subungual epithelial inclusion cyst

Intraosseous epidermoid cyst in animals was first described in the thoracic vertebral body of a dog by Liu and Dorfman (1974) and has also been reported in the mandible in horses (Camus et al., 1996). In the old WHO classification, the subungual cyst was previously categorized under the tumors of bones and joints as a very rare lesion (Misdorp and Heul, 1976). The authors give no reference as to previous publications on this subject, and the first possible publication on this type of cyst is reported by Bindseil et al. (1984).

This cyst is identical with the infundibular cyst and is found within the bone of the third phalanx (Goldschmidt et al., 1998). It is the most common skin cyst type of the toe in dogs (Frank et al., 1995) and probably arises from traumatically displaced epidermal cells (Jubb et al., 1993).

2.5.1.5.11. Dilated pore

This is a newly classified cyst, which was first described in man by Winer (1954), and in the cat by Scott and Flanders (1984). It is defined as a flasklike cystic structure with a wide external opening and laminated keratinaceous content (Luther et al., 1989), characterized by hyperplastic epithelium forming the deeper portion of the cyst wall (Goldschmidt et al., 1998). The outer wall of the cyst exhibits irregular hyperplasia, frequently with a scalloped configuration (Gross et al., 1992). It constitutes 9 % of all skin cysts of the cat (Luther et al., 1989).

2.5.1.5.12. Isthmus cyst

This is a newly classified cyst, named also isthmus-catagen cyst and tricholemmal cyst (Gross et al., 1992). It is defined as a simple cyst lined by keratinizing stratified squamous epithelium lacking a granular layer, which resembles the middle segment of the anagen follicle and the lower segment of the catagen follicle (Goldschmidt et al., 1998).

2.5.1.5.13. Panfollicular cyst

This is a newly classified cyst, named also trichoepitheliomatous cyst (Goldschmidt et al., 1998) and hybrid or mixed cyst (Gross et al., 1992), and it is characterized by two or three types of follicular differentiation in the same lesion (Scott et al., 2001). A third type of cell lining the cyst wall consists of primitive, small basophilic cells which show abrupt keratinisation to shadow cells (Goldschmidt et al., 1998). Small foci of inner root sheath differentiation with cells that have clear cytoplasm and trichohyalin granules may be present in the transitional zones (Gross et al., 1992, Goldschmidt et al., 1998).

2.5.1.5.14. Ciliated cyst

This is a newly classified cyst defined as a simple cyst lined by ciliated epithelial cells. Occasional goblet cells are interspersed between the ciliated cells (Goldschmidt et al., 1998), and the cyst contains a fluid (Goldschmidt and Shofer, 1992). This cyst represents a developmental defect of the thyroglossal ducts or respiratory tract and is found at the neck of cats (Goldschmidt and Shofer, 1992).

2.5.1.6. Hamartomas

This is a newly classified group, which was not found in the old WHO classification. Hamartomas are defined as circumscribed congenital lesions of the skin, characterized by hyperplasia of one or more skin components, and are commonly reported in dogs and cats (Scott et al., 2001). The term hamartoma was chosen to describe these lesions, rather than the term naevus, in order to avoid any possible confusion with the melanocytic nevi in humans (Goldschmidt et al., 1998). Despite this new nomenclature, some authors still use the term nevi (Scott et al., 2001). Hamartomas are subclassified into epidermal (pigmented epidermal naevus), follicular, sebaceous, apocrine and fibroadnexal hamartomas (adnexal naevus, focal adnexal dysplasia, folliculosebaceous hamartoma), which are congenital proliferations of benign epidermal cells, hair follicles, sebaceous glands, apocrine glands, and the pilosebaceous units with fibrous tissue, respectively (Goldschmidt et al., 1998).

2.5.1.7. Tumor-like lesions

This group is not found under the epithelial tumors of the old WHO classification; however, some tumor-like lesions are found in other groups such as sebaceous hyperplasia, which was categorized under sebaceous gland tumors (Weiss and Frese, 1974). The following seven types of epithelial tumor-like lesions are included in the new WHO classification:

2.5.1.7.1. Squamous papilloma

This is a newly classified tumor-like lesion defined as a non-neoplastic papillated mass composed of epidermis and supporting dermal stroma (Goldschmidt et al., 1998). This lesion should be distinguished from a viral papilloma (Goldschmidt and Hendrick, 2002) (Table 1).

Tab. 1: Differentiation between viral and squamous papilloma (Goldschmidt and Hendrick, 2002).

Viral papilloma	**Squamous papilloma**
Epidermal differentiation may show orthokeratosis or parakeratosis	Epidermal differentiation is normal
Enlarged keratohyaline granules	Normal size to keratohyaline granules
Koilocytes present	Koilocytes absent
Keratinocytes show viral cytopathic effect	Keratinocytes normal
Intranuclear inclusions may be present	No intranuclear inclusions
Elongated rete slant inward	Elongated rete slant outward
Dermal capillaries more prominent than in squamous papillomas	Dermal capillaries less prominent (Goldschmidt et al., 1998)

2.5.1.7.2. Pressure point comedones

Pressure point parts of the body are subject to pressure when the animal is recumbent, wears harness or saddlery, or during restraint. They are usually found in the bony prominences such as the point of the elbow (Blood and Studdert, 1999). Pressure point comedones are also a newly classified tumor-like lesion, which appear in the form of multiple simple cysts lined by the stratified squamous epithelium of the follicular infundibulum with accumulations of hair and keratin within the cyst lumina. These lesions occur primarily on the elbow (Goldschmidt et al., 1998).

2.5.1.7.3. Cutaneous horn

A newly classified tumor-like lesion, defined in the new WHO classification as a circumscribed exophytic lesion composed of dense, compact keratin with hyperplastic epidermis, which is primarily orthokeratotic and may include foci of parakeratosis (Goldschmidt et al., 1998). Many other authors define cutaneous horn as a general clinical term, and cutaneous horn may arise from many skin lesions such as papillomas, dilated pores, infundibular keratinizing acanthomas, basal cell tumors, squamous cell carcinomas, keratinous cysts, actinic keratosis (Gross et al., 1992, Scott et al., 2001) and Multicentric squamous cell carcinoma in situ (Rees and Goldschmidt, 1998).

2.5.1.7.4. Warty dyskeratoma

This is a newly classified tumor-like lesion, which is defined as isolated follicular dyskeratosis in human pathology (Murphy and Elder, 1990) and is a rare lesion in dogs (Scott et al., 2001). The term dyskeratosis is defined as premature and faulty keratinisation of individual cells, which can be seen in a number of inflammatory and neoplastic dermatoses (Jubb et al., 1993). Warty dyskeratoma is defined as a focal or multifocal endophytic proliferation of the epidermis exhibiting marked intralesional dyskeratosis and acantholysis (Goldschmidt et al., 1998).

2.5.1.7.5. Sebaceous hyperplasia

This lesion is also named senile nodular sebaceous hyperplasia (Weiss and Frese, 1974, Goldschmidt et al., 1998). It has been classified in both WHO classifications and is found under sebaceous gland tumors in the old WHO classification.

2.5.1.7.6. Fibroepithelial "polyp"

This lesion is also named cutaneous tag, skin tag and acrochordon (Goldschmidt et al., 1998). It has been classified in both WHO classifications and is found under tumor-like lesions of fibrous tissue in the old WHO classification, under the name of cutaneous fibrous polyp (Weiss, 1974). This lesion is very rare (Weiss, 1974, Gross et al., 1992) and sometimes known as pendulous soft fibroma (Jubb et al., 1993).

2.5.1.7.7. Fibropruritic nodule

This is a newly classified tumor-like lesion, which is also named neurodermatitis (Jubb et al., 1993) or acral lick granuloma (Goldschmidt et al., 1998). It forms focal or multifocal hyperplastic dermal nodules associated with chronic self-trauma and inflammation (Goldschmidt et al., 1998). This lesion is common in dogs, and has been among the 10 most common cases in one study of skin disease (Sischo et al., 1989). It is primarily found in limbs (White, 1990).

2.5.1.8. Melanocytic tumors

2.5.1.8.1. Melanocytoma and Malignant melanoma

Melanocytoma is also called dermal melanoma or benign melanoma (Goldschmidt et al., 1998). The old WHO classification of melanocytic tumors only referred to oral and skin melanomas in dogs (Weiss and Frese, 1974). Benign and malignant melanomas have been classified in both WHO classifications with some differences in their variants. For example, the balloon cell variant of the new WHO classification was not found in the old WHO classification, while the dendritic and whorled types in the old WHO classification have not been categorized in the new one (Weiss and Frese, 1974, Goldschmidt et al., 1998).

2.5.1.8.2. Melanoacanthoma

This is a newly classified melanocytic tumor, with features of a compound melanocytoma and of a benign epithelial neoplasm. It is a rare tumor in dogs (Goldschmidt et al., 1998), also called Melanocytoma-Acanthoma (Gross et al., 1992). This tumor was first reported and classified in dogs by Gross et al. (1992), without details as to age, breed and determination of site predilection. One other case was reported in a two-year-old female German shepherd dog, where it was located in the dermis of the dorsal trunk (Espinosa et al., 2000).

2.5.1.8.3. Melanocytic hyperplasia

This is a newly classified skin lesion that is also called lentigo, lentigo simplex (Goldschmidt et al., 1998) or macular melanosis (Scott et al., 2001). It is composed of a non-neoplastic proliferation of melanocytes within the epidermis, primarily in the basal cell layer (Goldschmidt et al., 1998). It was first described in dogs by Kraft and Frese (1976), and it is mostly found in female dogs, primarily in the last two mammary teats (Kraft and Frese, 1976a). Lentigo simplex, when present in orange cats, is usually found in animals younger than one year (Scott et al., 2001), and is represented by multifocal pigmentation of the lips, nose, gingiva, and eyelids (Nesbitt, 1998). A generalized lesion has been reported in a silver shorthair cat (Nash and Paulsen, 1990).

2.5.2. Mesenchymal Tumors of Skin and Soft Tissues

2.5.2.1. Tumors of Fibrous Tissue

This group has been classified in both WHO classifications (Weiss, 1974, Hendrick et al., 1998), with the following differences:

- Canine haemangiopericytoma was classified under “tumors of fibrous tissue” in the old WHO classification, and under “unclassified tumors” in the new one.
- Calcinosis circumscripta was classified under “tumors of fibrous tissue” in the old WHO classification, and reclassified under “miscellaneous tumors” in the new one.
- Cutaneous fibrous polyp was classified under “tumors of fibrous tissue” in the old WHO classification, while in the new WHO classification it is classified as fibroepithelial polyp under the category of epithelial tumor-like lesions.
- Undifferentiated sarcomas were classified under this group in the old WHO classification, but they have not been included in the new WHO classification.
- Keloid and hyperplastic scars were found in the old WHO classification and are absent in the new WHO classification.
- Sub-typing of fibrosarcoma into feline postvaccinal and canine well-differentiated maxillary and mandibular fibrosarcomas is found only in the new WHO classification.
- Collagenous hamartoma, nodular dermatofibrosis of the German shepherd dog, nodular fasciitis, myxosarcoma and malignant fibrous histiocytoma are found only in the new WHO classification.

2.5.2.1.1. Benign

2.5.2.1.1.1. Fibroma

Fibroma has two subtypes, fibroma durum (firm) and fibroma molle (soft) (Weiss, 1974, Scott et al., 2001). This sub-typing is not mentioned in the new WHO classification. Fibroma is defined as a benign tumor of mature fibrocytes producing abundant collagen (Hendrick et al., 1998).

2.5.2.1.1.2. Collagenous hamartoma

This common newly classified lesion was first distinguished from fibromas by Scott (1984). It is a nodular, poorly circumscribed focus of redundant collagen in the superficial dermis (Hendrick et al., 1998). This lesion has been recognized in many breeds of dogs (Hendrick et al., 1998, Scott et al., 2001).

Tab. 2: Comparison between collagenous hamartoma and fibroma (Gross et al., 1992)

	Collagenous hamartoma	**Fibroma**
Location	Superficial dermis	In the dermis and often encroach on the subcutis
Size	Usually less than 1 cm in diameter	Usually larger than collagenous hamartoma
Cellularity	Less cellular	More cellular
Growth form*	Lack of discrete growth habit, and often included trapped adnexae	Circumscribed nodule compresses adjacend structures
Pattern	Has a similar fiber pattern to that of the adjacent dermis	Repetitive, whirled or interlacing pattern of collagen fibers

* Wilcock and Yager (1994)

2.5.2.1.1.3. Nodular dermatofibrosis of the German shepherd dog

This is a newly classified lesion, also called multiple collagenous hamartoma (Scott et al., 2001). It is a rare breed-specific syndrome of multiple fibrous nodules in the dermis and subcutis (Hendrick et al., 1998) consisting of bundles of dense collagen fibers with few fibrocytes (Lium and Moe, 1985). Female German shepherd dogs are preferentially affected, but is has occasionally been found in other breeds (Hendrick et al., 1998). This lesion may coincide with unilateral or bilateral renal adenomas or carcinomas, with the presence of at least 30 to 50 nodules in the same animal and of several hundred in advanced cases. In these

advanced cases multiple leiomyomas are also mostly found in the uterus (Lium and Moe, 1985, Moe and Lium, 1997).

2.5.2.1.1.4. Nodular fasciitis

This is a newly classified non-neoplastic, enigmatic inflammatory lesion with many clinical and histological features suggestive of a locally invasive fibrosarcoma (Hendrick et al., 1998) or cutaneous histiocytosis (Goldschmidt and Hendrick, 2002). This lesion was first described in dogs by Bellhorn and Henkind (1967), and has also been reported in cats (Scott et al., 2001). It is most often found in the corneal and scleral regions of the eye, and in this site is also called nodular granulomatous episcleritis (Goldschmidt and Hendrick, 2002) or pseudosarcomatous fasciitis (Scott et al., 2001).

2.5.2.1.1.5. Myxoma

It has been classified in both WHO classifications (Weiss, 1974, Hendrick et al., 1998) and is also named myxofibroma (Weiss, 1974, Gross et al., 1992).

2.5.2.1.1.6. Equine sarcoid

This lesion has been classified in both WHO classifications (Weiss, 1974, Hendrick et al., 1998). It is the result of a non-productive infection with bovine papillomavirus in horses (Goldschmidt and Hendrick, 2002). The same lesion has been described in cats as follows:

Feline sarcoid:

It is a newly reported rare neoplasm, histologically resembling the equine sarcoid (Scott et al., 2001). An association with papillomavirus infection has been confirmed (Schulman et al., 2001), however, papillomavirus-DNA has been detected in mesenchymal tumor cells and not in the hyperplastic epithelium (Teifke et al., 2003). This tumor has been frequently reported as cutaneous fibropapilloma in cats (Gumbrell et al., 1998, Schulman et al., 2001, Hanna and Dunn, 2003), and similar lesions have been reported in the mouth of cats (Rest et al., 1997). Feline sarcoid has only recently been reported and is not found in either WHO classification.

2.5.2.1.2. Malignant

2.5.2.1.2.1. Fibrosarcoma

It is mentioned in both WHO classifications, with two new subtypes, one in cats and the other in dogs, which have both been described in the new WHO classification. These subtypes are

feline postvaccinal and canine well-differentiated maxillary and mandibular fibrosarcoma (Weiss, 1974, Hendrick et al., 1998).

2.5.2.1.2.2. Myxosarcoma

It is a newly classified tumor arising from primitive pleomorphic fibroblasts which produce excessive mucin (Hendrick et al., 1998). However, only the benign tumor was classified in the old WHO classification.

2.5.2.1.2.3. Malignant fibrous histiocytoma

This is a newly classified tumor (Hendrick et al., 1998) also named extraskeletal giant cell tumor, giant cell tumor of soft parts or dermatofibrosarcomas. It is uncommon in cats, rare in dogs (Scott et al., 2001). This tumor has a high rate of metastasis (90%) (Waters et al., 1994) and has many different variants: storiform-pleomorphic, inflammatory and giant cell variants. This tumor presumably arises from primitive mesenchymal cells, shows evidence of a fibroblastic/myofibroblastic phenotype (Hendrick et al., 1998), and its relation with malignant histiocytosis has been discussed (Kerlin and Hendrick, 1996). A benign variant in dogs and cats has been described (Scott et al., 2001). It has not been classified in the new WHO classification. In humans, malignant fibrous histiocytoma is the most common soft tissue tumor of adults (Murphy and Elder, 1990).

2.5.2.2. Tumors of Adipose Tissue

Lipoma and liposarcoma were classified in the old WHO classification, however, many variants were not described there, and other variants are not mentioned in the new WHO classification (Weiss, 1974, Hendrick et al., 1998).

2.5.2.2.1. Benign

2.5.2.2.1.1. Lipoma

Lipoma is mentioned in both WHO classifications. The infiltrative lipoma is a newly added variant (Hendrick et al., 1998) that is uncommon in dogs and rare in cats (Gross et al., 1992). Infiltrative lipoma has a high recurrence rate (Bergman et al., 1994, McChesney et al., 1980) and may result from trauma to a simple lipoma (McChesney et al., 1980).

Other lipomas such as myxoid lipoma (Weiss, 1974), fibrolipoma (Gross et al., 1992), chondrolipoma (Goldschmidt and Shofer, 1992) intermuscular lipoma (Thomson et al., 1999), and pigmented lipoma (Scott et al., 2001) are not described in the new WHO classification.

2.5.2.2.1.2. Angiolipoma

This is a newly classified variant of lipoma consisting of small, well-differentiated blood vessels within the tumor. This tumor is rare and is found in dogs, but has also been reported in cats (Hendrick et al., 1998, Liggett et al., 2002).

2.5.2.2.2. Malignant

2.5.2.2.2.1. Liposarcoma

Two variants have been classified in both WHO classifications: well differentiated and pleomorphic liposarcomas (Weiss, 1974, Hendrick et al., 1998). The myxoid variant is a newly classified one that is identified by the presence of scattered lipoblasts and a bubbly appearance to the stromal mucin (Hendrick et al., 1998) and it has been reported in dogs (Messick and Radin, 1989).

2.5.2.3. Tumors of Smooth Muscle

This group has been classified in both WHO classifications with few differences and includes leiomyoma and leiomyosarcoma (Weiss, 1974, Hendrick et al., 1998). The variant called mixed fibroleiomyoma is included only in the new WHO classification. Fibroleiomyomas are commonly seen in the female genital tract (Hendrick et al., 1998), however, dermal tumor has also been reported (Liu and Mikaelian, 2003).

Arrector pili hamartoma, angioleiomyoma and angioleiomyosarcoma have been recently reported in dogs and cats (Liu and Mikaelian, 2003), and are not described in the new WHO classification.

2.5.2.4. Tumors of Striated Muscle

This group has been categorized in both WHO classifications with few differences, and includes rhabdomyoma and rhabdomyosarcoma (Weiss, 1974, Hendrick et al., 1998). A variant of rhabdomyosarcoma named embryonal rhabdomyosarcoma of the urinary bladder is only described in the new WHO classification (Hendrick et al., 1998). This tumor variant is also called botryoid sarcoma or sarcoma botryoides (Kuwamura et al., 1998, Takiguchi et al., 2002).

2.5.2.5. Tumors of Vascular Tissue

2.5.2.5.1. Benign

Hemangioma and lymphangioma have been described in both WHO classifications (Weiss, 1974, Hendrick et al., 1998).

Scrotal vascular hamartoma in the new WHO classification was also described under this group in the old WHO classification as a tumor-like lesion; it shows varicosis and ectasia of scrotal veins. This lesion is similar to angiokeratoma (Mibelli) of man (Weiss, 1974).

Cutaneous bovine angiomatosis is a newly classified lesion (Hendrick et al., 1998) that was reported early (Cotchin and Swarbrick, 1963) but was not described in the old WHO classification. This lesion is found in the skin and most other organs in bovine (Watson and Thompson, 1990). This lesion is also known as vascular hamartoma (Sheahan BJ, Donnelly, 1981), angiomatous vascular malformation (Cho et al., 1979) and as hemangiomas (Kirkbride et al., 1973). A similar lesion to cutaneous bovine angiomatosis has also been reported in canine (Kim et al., 2005).

Angiokeratoma is a rare variant of hemangioma in dogs, containing both vascular and epithelial components. It occurs most often on the eyelid and conjunctiva, but can also arise in the superficial dermis at any site (Yager and Wilcock, 1994, Vala and Esteves, 2001). However, this tumor has not been mentioned in either WHO classification.

2.5.2.5.2. Intermediate

2.5.2.5.2.1. Kaposi-like vascular tumor

It is a newly classified tumor (Hendrick et al., 1998). Only few cases have been reported in female dogs (Goldschmidt and Hendrick, 2002) and in one male dog (Vincek et al., 2004).

2.5.2.5.3. Malignant

Hemangiosarcoma and lymphangiosarcoma are described in both WHO classifications (Weiss, 1974, Hendrick et al., 1998).

One variant in cats, named feline ventral abdominal angiosarcoma is mentioned in the new WHO classification. The tumor origin, from blood vessel or lymphatic vessel, is controversial (Hendrick et al., 1998). Some publications have confirmed that this tumor is of lymphatic origin, and they recommend using the term feline ventral abdominal lymphangiosarcoma (Swayne et al., 1989, Galeotti et al., 2004).

Epithelioid haemangioendothelioma, which has been described in the skin and in some other organs in humans (Weiss and Bridge, 2002), has also been reported in the lung of a dog (Machida et al., 1998). This type of tumor is not mentioned in the new WHO classification.

2.5.2.6. Tumors of Peripheral Nerves

This group of tumors is found in both WHO classifications, with different nomenclatures. The old WHO classification describes three tumor types: neurinoma (schwannoma), neurofibroma, and neurofibrosarcoma (Weiss, 1974). However, the new WHO classification renames schwannoma and neurofibroma together as benign peripheral nerve sheath tumors of the skin and subcutis, and neurofibrosarcoma is renamed malignant peripheral nerve sheath tumor of the skin and subcutis. Together with these, two new lesions were described in the new WHO classification, namely traumatic neuroma and granular cell tumor (Hendrick et al., 1998).

Traumatic neuroma is described as a non-neoplastic lesion that occurs after transection of a nerve by trauma or surgery (Hendrick et al., 1998).

2.5.2.6.1. Granular cell tumor

It is the most frequently reported primary lung tumor of horses, and it has also been reported in dogs, cats and birds (Pusterla et al., 2003). It is also called granular cell myoblastoma (Cooper and Valentine, 2002), myoblastoma or putative Schwann cell tumor (Pusterla et al., 2003). The histogenesis of granular cell tumor has remained unresolved since the original description by Abrikossoff (1926). It was believed to be of skeletal muscle, smooth muscle, endothelial, perineural fibroblasts, perineural epithelial, or epithelial cells (Patnaik, 1993). It is mentioned under tumors of peripheral nerves in the new WHO classification because of its presumptive Schwann cell origin (Hendrick et al., 1998). Some other authors mention this tumor as a neoplasm of uncertain origin (Cooper and Valentine, 2002)

2.5.2.7. Tumors of Synovium

This group is found in both WHO classifications, and in the old WHO classification was classified under tumors of bones and joints as tumors of joints and related structures, which included synovial sarcoma, fibrous histiocytoma and malignant giant cell tumor of soft tissue (Misdorp and Van Der Heul, 1976). In the new WHO classification, it is mentioned under the tumor group of bones and joints as well as under mesenchymal tumors of the skin and soft tissues (Hendrick et al., 1998). According to the new WHO classification, this group consists

of only one tumor, the synovial sarcoma. Primary tumors of the synovium are uncommon in dogs. However, synovial sarcomas occur most frequently in the stifle joint (Harasen, 2002). In a recent study, the most common primary synovial tumors are histiocytic sarcomas (more than 51 %), while only 14 % are recognized as synovial cell sarcomas. In addition, myxosarcomas and fibrosarcomas are also described as primary synovial tumors (Craig et al., 2002), and these tumors are not included under the synovial tumors in the new WHO classifications.

2.5.2.8. Tumors of Mesothelium

This group has been newly classified in the WHO classification under different organs, skin and soft tissues (Hendrick et al., 1998), alimentary (Head et al., 2003) and respiratory system (Dungworth et al., 1999). These tumors are not found in all the groups and organs of the old WHO classification, and according to the new WHO classification comprise only mesothelioma. This tumor is rare, intermediate in malignancy (Hendrick et al., 1998) and frequently reported in cattle (Wolfe et al., 1991, Beytun, 2002). It has also been recorded in dogs and cats (Head et al., 2002).

2.5.2.9. Mast Cell Tumors

It is named also mastocytoma, and has been described only as a malignant skin tumor (Weiss, 1974). In the new WHO classification, it is classified according to animal species (Hendrick et al., 1998). The classification into well-differentiated, poorly differentiated, and malignant mastocytosis was found under tumors of haematopoietic and lymphoid tissues in the old WHO classification (Jarrett and Mackey, 1974).

2.5.2.9.1. Feline

Mast cell tumor is the second most common skin tumor in the cat (Miller et al., 1991) and it is mostly benign (Hendrick et al., 1998). There is no grading as in dogs, and the cellular pleomorphism alone is not indicative of an aggressive behavior of the cutaneous mast cell tumor (Johnson et al., 2002). However, mitotic activity seems to be the most effective prognostic tool for feline cutaneous mast cell tumor (Johnson et al., 2002, Lepri et al., 2003).

2.5.2.9.1.1. Feline, "histiocytic"

It is mentioned in the new WHO classification (Hendrick et al., 1998). It is a rare variant, which occurs mostly in young Siamese cats (Wilcock et al., 1986, Hendrick et al., 1998,

Goldschmidt and Hendrick, 2002). It has also been reported in Himalayan (Larocca, 2000) and in Persian cats (Wilcock et al., 1986) and is mostly benign (Wilcock et al., 1986, Lepri et al., 2003) and may be regressed (Wilcock et al., 1986). The overall appearance of this tumor is granulomatous (Wilcock et al., 1986, Gross et al., 1992, Hendrick et al., 1998).

Another variant, the pleomorphic cutaneous mast cell tumor with mostly benign behaviour, has been reported (Johnson et al., 2002) and is not categorized in the new WHO classification.

2.5.2.9.2. Canine

Mast cell tumor is the most common mesenchymal cutaneous neoplasm of dogs, as mentioned in the old WHO classification, in contrast to the new one, which describes histiocytomas as the most common canine skin tumor (Weiss, 1974, Hendrick et al., 1998). It is a malignant tumor that can develop in many other organs. The main change with regard to this tumor is the grading system (I, II, III) in the new WHO classification (Hendrick et al., 1998). The grading is histomorphologic and has great significance for the assessment of the survival time of the affected animals (Patnaik et al., 1984).

2.5.2.9.3. Mast cell tumor in other species

Mast cell tumors occasionally arise in horses, cattle, pigs, and ferrets (Hendrick et al., 1998, Goldschmidt and Hendrick, 2002), and have also been reported in donkeys and mules (Kay et al., 2003).

2.5.2.10. Histiocytic Tumors

The old WHO classification mentions only canine cutaneous histiocytoma. Reticulosarcoma (cutanous reticulosis) is also mentioned as a tumor resembling malignant histiocytic neoplasm, and it is suspected to be of lymphocytic origin (Weiss, 1974); it has later been designated atypical histiocytoma, and has been confirmed as a cutaneous plasmacytoma (Baer et al., 1989, Rakich et al., 1989, Gross et al., 1992).

Histiocytic sarcoma is also called localized histiocytic sarcoma (Scott et al., 2001). Rottweilers and Bernese mountain dogs are mainly affected, and it is more often found in the skin and skeletal muscles than in other organs (Affolter and Moore, 2002). It has been classified by Scott et al. (2001), but is not included in either WHO classification.

Atypical histiocytoma that is histologically similar to benign cutaneous histiocytoma has been reported by Kipar (1994), but it is not mentioned in either WHO classification.

2.5.2.10.1. Canine cutaneous histiocytoma

It is the most common cutaneous neoplasm of dogs in the new WHO classification, in contrast to the old WHO classification, which described mast cell tumor as the most common mesenchymal skin tumor (Weiss, 1974, Hendrick et al., 1998).

2.5.2.10.2. Xanthoma and cutaneous histiocytosis

They are not to be found in the old WHO classification (Weiss, 1974). Cutaneous histiocytosis is classified under intermediate histiocytic tumors in the new WHO classification (Hendrick et al., 1998). However, both lesions have been described as non-neoplastic lesions by Goldschmidt and Hendrick (2002).

2.5.2.10.3. Systemic histiocytosis

A newly classified tumor that is limited to the Bernese mountain dog (Hendrick et al., 1998, Scott et al., 2001).

2.5.2.10.4. Malignant histiocytosis

This is a newly classified tumor (Hendrick et al., 1998) also called disseminated histiocytic sarcoma (Scott et al., 2001), which mostly affects Rottweilers and Bernese mountain dogs. This tumor has more often been found in the internal organs than in the skin (Affolter and Moore, 2002) and has also been reported in cats (Gafner and Bestetti, 1988, Court et al., 1993).

2.5.2.11. Miscellaneous Tumors

This group is found in both WHO classifications under the same name, but with totally different tumor types. This group consists of cutaneous lymphosarcoma and canine transmissible venereal tumor in the old WHO classification (Weiss, 1974). Meanwhile, only calcinosis circumscripta is described in the new WHO classification (Hendrick et al., 1998).

2.5.2.11.1. Benign

2.5.2.11.1.1. Calcinosis circumscripta

This lesion is mentioned in both WHO classifications in different categories. In the old WHO classification, it was mentioned as a tumor-like lesion under tumors of fibrous tissue. This lesion has been described in dogs (Weiss, 1974, Hendrick et al., 1998) and cats (Scott et al., 2001, Head et al., 2002).

In the new WHO classification, it is described as a lesion identical with tumoral calcinosis in humans (Hendrick et al., 1998). However, the designation is not accepted by Pool and Thompson (2002), who prefer to use the term multicentric periarticular calcinosis in animals for a lesion that looks like tumoral calcinosis in humans. Multicentric periarticular calcinosis can only be distinguished from calcinosis circumscripta by its para-articular location (Pool and Thompson, 2002). Calcinosis circumscripta is also called apocrine cystic calcinosis, multiloculated subcutaneous granuloma (Bettini et al., 2005) or calcium gout (Head et al., 2002).

2.5.2.12. Unclassified Tumors

This group is found in both WHO classifications; however, the old WHO classification gives no further details (Weiss, 1974, Hendrick et al., 1998).

2.5.2.12.1. Malignant

2.5.2.12.1.1. Canine hemangiopericytoma

This tumor was classified under fibrosarcomas in the old WHO classification, and it is also called fibrosarcoma with perithelioma-like structures, perithelioma, haemangiosarcoma (Weiss, 1974), and spindle cell tumor of canine soft tissue (Yager and Wilcock, 1994). The actual histogenesis is uncertain (Hendrick et al., 1998, Goldschmidt and Hendrick, 2002) despite ultrastructural and immunohistochemical confirmation of the pericytic origin (Xu, 1986, Perez, 1996). This tumor is mainly found in dogs, but there are other tumors with a similar morphology, which rarely occur in cats and are most likely of peripheral nerve sheath origin (Goldschmidt and Hendrick, 2002). Hemangiopericytoma is an uncommon neoplasm in humans and its pericytic origin has been confirmed ultrastructurally (Enzinger and Weiss, 1995).

2.5.2.12.1.2. Malignant mesenchymoma

It has occasionally been seen in the spleen, and even less frequently in the subcutis and retroperitonium (Hendrick et al., 1998). This term is found in both WHO classifications in different locations and with some differences in definitions. In the old WHO classification, it is found under miscellaneous tumors of the bone and defined as a malignant tumor consisting of both osteosarcomatous and liposarcomatous tissues, also named osteoliposarcoma (Misdorp and Van der Heul, 1976). In the new WHO classification, this tumor is found under miscellaneous tumors of the bone and joint and defined as a malignant tumor characterized by

the presence of multiple types of differentiation such as osteosarcomatous and liposarcomatous (Slayter et al., 1994). It is also classified under mesenchymal tumors of the skin and soft tissues and can have regions of more than two mesenchymal cell types and contain well-differentiated leiomyosarcoma, osteosarcoma and liposarcoma in the same neoplasm. Collision tumors and poorly differentiated tumors are not included in this category (Hendrick et al., 1998).

3. MATERIALS AND METHODS

We collected 816 skin tumors and tumor-like lesions from 768 dogs, and 194 skin tumors and tumor-like lesions from 194 cats. All the sections and data were in the archives of institute of veterinary pathology at Justus-Liebig-University, Giessen, Germany. The biopsies were received at the institute between January and April 2000 for diagnostic purposes. Biopsies were fixed in 10% formalin, processed (Tissue Tek® Vacuum infiltration processor, Fa. Vogel Wilhelm GmbH, Giessen), embedded in paraffin (Histo-Comp® tissue embed device, Fa. Vogel Wilhelm GmbH, Giessen), sectioned at 4 μm thickness (Rotation microtome HM340 E, Fa. Microm Laborgeraete GmbH, Walldorf; Microtome blade: Stainless steel S35, Fa. Feather Safety Razor Co., Ltd. Medical Division, Japan) and stained with Haematoxylin and Eosin (HE), then covered with foil in the covering machine (TissueTec®, Mod. 4765, Vogel Wilhelm GmbH, Giessen). Some sections were stained additionally with other special stains including Periodic Acid Schiff stain (PAS), Toluidin and Masson's trichrome stains. In some cases melanin bleach was used.

Immunohistological techniques were also applied for the identification of cytokeratin, vimentin, actin, desmin, S100, neurofilament, Melan A, neuron specific enolase (NSE), synaptophysin, CD79α and smooth muscle actin using the avidin-biotin complex (ABC) method, and glial fibrillary acidic protein (GFAP), factor VIII-related antigen, MHC II, lysozyme, CD3, CD45R and MAC387 using the peroxidase-antiperoxidase (PAP) method.

Diagnosis was registered at that time according to the old WHO classification of the tumors of the skin and soft tissues (Weiss and Frese, 1974, Weiss, 1974). Sections were looked at twice again, and rediagnosed according to the new WHO classification of the tumors of the skin and soft tissues (Goldschmidt et al., 1998, Hendrick et al., 1998). Data were registered in Excel-table format.

3.1. Hematoxylin and Eosin (HE): Stain Protocol for Shandon Varistain 24-3

Sections: Sections from paraffin blocks were attached to glass slides (Star Frost® geschnitten, Fa. Engelbrecht Medizin- und Labortechnik GmbH, Edermuende), dried at room temperature, and then deparaffinized. The deparaffinization process took place in the staining machine as described in the staining procedure below.

Solutions:

Kardasewitsch solution (5 % alcoholic ammonia solution):

25 % ammonia solution, mix with 4 times the volume of 70% ethanol

Eosin solution:

300 ml stock solution

20 g eosin (Eosin, Fa. Carl Roth GmbH & Co KG, Karlsruhe), dilute in 1000 ml distilled water and 1000 ml 2-propanol

300 ml distilled water

300 ml ethanol 96 %

1 ml glacial acetic acid (acetic acid Rotipuran® > 99.7 %, Fa. Carl Roth GmbH & Co KG, Karlsruhe)

Hematoxylin:

100 ml hematoxylin (Papanicolaous-solution 1b hematoxylin solution S, Fa. Merck KGaA, Darmstadt) mixed with 400 ml distilled water

HCl-alcohol (acid alcohol 1 %):

99 ml 70% alcohol mixed with 1ml conc. hydrochloric acid (hydrochloric acid 32 % Carl Roth GmbH & Co. KG, Karlsruhe)

Procedure:

This process runs in the staining machine (Varistain 24-3, Fa. Shandon GmbH, Frankfurt am Main) as follows:

Step	**Substance**	**Time [Min:Sec]**
1	Xylene isomer >98 %	2:00
2	Xylene isomer >98 %	2:00
3	Isopropanol (2-Propanol)	2:00
4	Isopropanol (2-Propanol)	2:00
5	Ethanol 96 %	2:00
6	Ethanol 96 %	1:00
7	Ethanol 70%	0:30
8	5 % Ammonia solution (Kardasewitsch)	4:00
9	Tap water	4:00
10	Tap water	2:00
11	Hematoxylin	4:00
12	Tap water	5:00
13	Acid alcohol 1 % (HCL-Alcohol)	0:01
14	Eosin	1:30
15	Ethanol 96 %	1:00
16	Ethanol 96 %	0:30
17	Ethanol 96 %	0:30
18	Isopropanol	0:30
19	Isopropanol	0:30
20	Xylene isomere	0:30
21	Xylene isomere	0:30
22	Xylene isomere	0:30
23	Covering	

Results:

Nuclei: Blue-black

Cytoplasm: Varying shades of pink

Muscle fibers: Deep pinky red

Fibrin: Deep pink

Red blood cells: Orange/red

3.2. Special stains

Deparaffinize:

Slides from paraffin blocks were deparaffinized just prior to special staining as follows:

1. Rinse 5 min in xylene
2. Rinse 5 min in absolute isopropanol
3. Rinse 5 min in 96 % ethanol
4. Rinse 5 min in 70% ethanol
5. Rinse 5 min in 50% isopropanol
6. Rinse briefly in distilled water

3.2.1. Periodic Acid Schiff stain (PAS) with or without pre-processing with diastase

Sections: Deparaffinized sections

Solutions:

Diastase treatment (Saliva)

0.5 % aqueous periodic acid solution

Graumann's Schiff reagent:

5 g P-rosanilin acridene-free in 150 ml 1 normal HCl solution. Add 850 ml distilled water with 5 g potassium disulfide. The solution becomes yellowish within 24 hours, then shake for 2 min with 3 g active coal. This working solution is stable for 2 months (keep in refrigerator).

Sulfide water:

300 ml distilled water

15 ml 10% potassium disulfide ($K_2S_2O_5$, Merck KGaA, Darmstadt)

15 ml 1 normal HCl

Pre-processing with diastase:

Dip in diastase at room temperature for 2 hours

Procedure:

Steps	Substance	Time [Min:Sec]
1	Periodic acid solution 0,5 %	10:00
2	Rinse with tap water	10:00
3	Rinse with distilled water	2 x 2:00
4	Schiff reagent (at 60 C°)	30:00
5	Fresh sulfide water	3 x 2:00
6	Rinse with tap water	10:00
7	Rinse with distilled water	2:00
8	Haemalaun	3:00
9	Rinse with tap water	3:00
10	50% isopropanol	3:00
11	70% isopropanol	3:00
12	96 % ethanol	3:00
13	Absolute isopropanol	2 x 3:00
14	Xylene	3:00
15	Covering	

Results:

PAS positive: stained red (Polysaccharide and neutral muco-substances)

Diastase resistant: stained red

Diastase not resistant: not stained (Glycogen)

3.2.2. Toluidin

Sections: Deparaffinized sections

Solutions:

1 % toluidin blue (aqueous) (Dr. K. Hollborn & Soehne GmbH & Co KG, Leipzig), 96 % ethanol with two drops of glacial acetic acid, absolute alcohol and xylene.

Procedure:

Stain one hour with 1 % toluidin blue, then differentiate in 96 % alcohol mixed with two drops of glacial acetic acid, dip briefly in absolute alcohol.

Rinse for 5 min in xylene, then cover

Results:

Mast cells and some mucins: Purple/red

Nuclei: Pale blue

3.2.3. Masson's trichrome

Sections: Deparaffinized sections

Solutions:

Weigert's iron hematoxylin solution (Carl Roth GmbH & Co. KG, Karlsruhe)

Acid fuchsin solution:

1 g acid fuchsin (Carl Roth GmbH & Co. KG, Karlsruhe)

1 ml glacial acetic acid (Carl Roth GmbH & Co. KG, Karlsruhe)

100 ml distilled water

Phosphomolybdic acid solution:

1 g phosphomolybdic acid (Carl Roth GmbH & Co. KG, Karlsruhe)

100 ml distilled water

Aniline blue solution:

2.5 g aniline blue (Carl Roth GmbH & Co. KG, Karlsruhe)

2.5 ml glacial acetic acid (Carl Roth GmbH & Co. KG, Karlsruhe)

100 ml distilled water

1 % acetic acid solution:

1 ml glacial acetic acid (Carl Roth GmbH & Co. KG, Karlsruhe)

99 ml distilled water

Procedure:

1. Stain in Weigert's iron hematoxylin solution for 5 min
2. Rinse briefly in running tap water
3. Differentiate in 1 % acetic acid until the connective tissue is approximately colorless
4. Rinse in distilled water, 2 x 5 min
5. Stain in acid fuchsin solution for 5 min

   One part A (1 g acid fuchsin, 100 ml distilled water and 1 ml glacial acetic acid)

   Two parts B (1 g ponceau de xylidine on 100 ml distilled water and 1 ml glacial acetic acid)
6. Rinse briefly in distilled water
7. Differentiate in 1 % phosphomolybdic acid solution for 5 min
8. Transfer sections directly (without rinse) into 1 % aniline blue solution and stain for 1.5

min

9. Rinse briefly twice in distilled water and dip in glacial acetic acid for 5 min, then dip for 3 minutes in absolute alcohol

10. Rinse 5 min in xylene, then cover

Results:

Collagen: Blue

Nuclei: Black

Muscle, cytoplasm, keratin: Red

3.2.4. Melanin bleach

Sections: Deparaffinized sections

Solutions:

1 % potassium permanganate ($KMnO_5$, Merck KGaA, Darmstadt)

2 % potassium disulfide ($K_2S_2O_5$, Merck KGaA, Darmstadt)

Procedure:

Treat sections with 1 % potassium permanganate for 30 min

Rinse in water

Treat sections with 2 % potassium disulfide for 20 min

Rinse in running water, examine and re-bleach if necessary until the sections become white

Counterstain in hematoxylin and eosin (HE) as follow:

3 min haemalaun (Carl Roth GmbH & Co. KG, Karlsruhe)

3 min rinse under running tap water

10 min eosin (Carl Roth GmbH & Co. KG, Karlsruhe)

Dip briefly in ascending alcohol concentrations (1 sec each) as follows:

50% isopropanol (Carl Roth GmbH & Co. KG, Karlsruhe)

70% isopropanol (Carl Roth GmbH & Co. KG, Karlsruhe)

96 % ethanol (Carl Roth GmbH & Co. KG, Karlsruhe)

Absolute isopropanol

Rinse briefly in xylene, then cover

3.3. Immunhistology

For the immunohistological examination, sections of 2-3 µm thickness on SuperFrost®/Plus slides (041300, Menzel Glaeser Braunschweig) were prepared and afterwards dehydrated for at least one hour in front of the ventilator or over night at room temperature.

Swine, rabbit, horse and rat serum:

Keep the blood of swine, rabbits, horses and rats for 2 to 4 hours at room temperature, then centrifuge for 10 min at 1500 rpm to collect the serum. Filtrate the serum to be sterile, conserve by adding 0.05 % merthiolate and store at -20°C.

Shandon Coverplate™ Technology:

The Shandon Coverplate (Thermo Electron Co., Dreieich) is a plastic device that fits over a standard microscope slide allowing specimens to be immunostained with a minimum amount of reagent. This technology was used in our immunohistological staining.

3.3.1. General processes

Many processes were identical in all types of immunhistological staining procedures used in our study. These are described in the following. The specificities of the different types of immunohistological staining in our study are each described thereafter.

3.3.1.1. Deparaffinize

Slides from paraffin blocks were deparaffinized as follows:

1. Rinse three times, 3 min each in xylene
2. Rinse two times, 3 min each in isopropanol
3. Rinse 3 min in 96 % ethanol
4. Rinse 3 min in 80% ethanol

3.3.1.2. Inhibition of the endogeneous peroxidase

Incubate for 30 min at room temperature in methanol with 0.5 % fresh H_2O_2 (30%)

3.3.1.3. Pre-processing

3.3.1.3.1. Protease

5 min NaCl - PBS (pH: 7.4, 0.15 M) at 37°C in incubator

5 min 0.05 % protease (Type XXIV) (Sigma-Aldrich Chemie GmbH, Taufkirchen) solved in NaCl – PBS (pH: 7.4, 0.15 mol/l) 37°C

3 x 5 min ice-cold TBS to stop the reaction

3.3.1.3.2. Citrate

Citrate buffer (pH: 6,0, 10 mM): preheat to 97°C and set slides in the solution for 10-15 min.

Cool slides down in the solution at room temperature for 15 min, then convert in TBS

3.3.1.4. Dilute the antibody

Dilute the antibody in TBS with 1 % BSA as in table 3:

Tab. 3: Antibody dilution

Antibody and negative contro	Pre-dilution	Dilution
Anti-cytokeratin	--	1:50
T_1 (negative control)	--	1:50
Anti-vimentin	--	1:50
T_1 (negative control)	--	1:50
Anti–muscle actin	--	1:200
T_1 (negative control)	--	1:200
Anti-desmin	--	1 : 800
T_1 (Negative control)	--	1 : 800
Anti-neurofilament	--	1 : 400
T_1 (negative control)	--	1 : 400
Anti-GFAP	--	1 : 500
KK (negative control)	--	1 : 1829
Anti – melan A	--	1 : 25
TBS with 1 % BSA (negative control)	--	--
Anti – factor VIII	--	1 : 1000
KK (negative control)	1:10	1 : 2631
Mouse anti-MHCII	--	1 : 25
T1 (negative control)	--	1 : 25
Anti - lysozyme	--	1 : 600
KK (negative control)	1:10	1 : 1285
Anti - CD3	--	1 : 200
Rabbit serum (negative control)	1:10	1 : 6000
Anti – CD45R	--	1 : 1000
T1 (negative control)	--	1 : 1000
Anti-CD79 αcy	--	1 : 50
T1 (negative control)	--	1 : 50
Anti-NSE	--	1 : 100
T1 (negative control)	--	1 : 100
Anti-synaptophysin	--	1 : 100
T1 (negative control)	--	1 : 100
Anti – S100	--	1 :400
KK (negative control)	1:10	1 :133
Anti–MAC387	--	1 :1000
T1 (negative control)	--	1 :1000
Anti-smooth muscle actin	--	1 : 500
T_1 (negative control)	--	1 : 500

3.3.1.5. General processes after incubation with the ABC complex or the PAP complex

1) Rinse 3 x 5 min in TBS with 1 % BSA buffer

2) Incubate all slides for 10 min at room temperature and under constant stirring in fresh and filtrated DAB (0.05 % DAB in 0.1 M imidazol/HCl buffer pH: 7.08 with 0.01 % H_2O_2 (30%))

3) Rinse for 3 x 5 min in TBS

4) Rinse for 1 x 5 min in distilled water

5) Rinse 5 min in Kardasewitch, then rinse thoroughly in distilled water

6) Counterstain with papanicolaous hematoxylin (1:10, dilute in distilled water), duration according to desired color intensity

7) Rinse for 5 min in tap water and for 1 min in distilled water

8) Dehydrate and cover

Slides should be dehydrated and covered at the end of the following process:

Rinse 3 min in 50% ethanol

Rinse 3 min in 70% ethanol

Rinse 3 min in 80% ethanol

Rinse 3 min in 96 % ethanol

Rinse 2 x 3 min in isopropanol

Rinse 3x 3 min in rotihistol

Rinse 10 min in xylene, and then cover in covering-machine (TissueTec®, Mod. 4765, Vogel Wilhelm GmbH, Giessen)

3.3.2. Immunhistological stains

3.3.2.1. Cytokeratin

Antibody: Mouse anti-cytokeratin pan (clone: Lu5)

Provenance: Neomarkers Dunn Labortechnik GmbH, Asbach

Sections: Deparaffinized sections (see 3.3.1.1.)

Procedure:

1) Inhibition of the endogeneous peroxidase (see 3.3.1.2.)

2) Rinse for 5 min in TBS

3) Pre-processing with Protease (see 3.3.1.3.1.)

4) Insert slides in Shandon Racks

5) Blocking serum for 10 min at room temperature, horse serum.

6) Incubate primary antibody over night at 4°C in the refrigerator

Dilute the antibody in TBS with1 % BSA (see 3.3.1.4.)

7) Rinse 3 x 5 min in TBS buffer

8) Incubate the secondary antibody for 30 min at room temperature, Biotinylated Horse anti-Mouse IgG (H+L)

Preparation: 9 µl for 1 ml TBS with 1 % BSA buffer

9) Rinse the sections 3 x 5 min in TBS buffer

10) Incubate the ABC complex for 30 min at room temperature

Preparation: 9 µl Avidin + 9 µl Biotin for 1 ml TBS buffer

Attention! It has to be prepared 30 min before use

11) Then as above (see 3.3.1.5.)

3.3.2.2. Vimentin

Antibody: Mouse anti-vimentin (clone V9)

Provenance: Dako Cytomalion GmbH, Hamburg

Sections: Deparaffinized sections (see 3.3.1.1.)

Procedure:

1) Inhibition of the endogeneous peroxidase (see 3.3.1.2.)

2) Rinse for 5 min in TBS

3) Insert slides in Shandon Racks

4) Blocking serum for 10 min at room temperature, horse serum.

5) Incubate primary antibody over night at 4°C in the refrigerator

Dilute the antibody in TBS with1 % BSA (see 3.3.1.4.)

6) Rinse 3 x 5 min in TBS buffer

7) Incubate the secondary antibody for 30 min at room temperature, Biotinylated Horse anti-Mouse IgG (H+L)

Preparation: 9 µl for 1 ml TBS with1 % BSA buffer

8) Rinse the sections 3 x 5 min in TBS buffer

9) Incubate the ABC complex for 30 min at room temperature

Preparation: 9 µl Avidin + 9 µl Biotin for 1 ml TBS buffer

Attention! It has to be prepared 30 min before use

10) Then as above (see 3.3.1.5.)

3.3.2.3. Actin

Antibody: Mouse anti-actin (clone HHF-35)

Provenance: Dako Cytomation GmbH, Hamburg

Sections: Deparaffinized sections (see 3.3.1.1.)

Procedure:

1) Inhibition of the endogeneous peroxidase (see 3.3.1.2.)

2) Rinse for 5 min in TBS

3) Insert slides in Shandon Racks

4) Blocking serum for 10 min at room temperature, horse serum.

5) Incubate primary antibody over night at 4°C in the refrigerator

Dilute the antibody in TBS with 1 % BSA (see 3.3.1.4.)

6) Rinse 3 x 5 min in TBS buffer

7) Incubate the secondary antibody for 30 min at room temperature, Biotinylated Horse anti-Mouse IgG (H+L)

Preparation: 9 µl for 1 ml TBS with 1 % BSA buffer

8) Rinse the sections 3 x 5 min in TBS buffer

9) Incubate the ABC complex for 30 min at room temperature

Preparation: 9 µl Avidin + 9 µl Biotin for 1 ml TBS buffer

Attention! It has to be prepared 30 min before use

10) Then as above (see 3.3.1.5.)

3.3.2.4. Desmin

Antibody: Mouse anti-desmin (clone D33)

Provenance: Dako Cytomation GmbH, Hamburg

Sections: Deparaffinized sections (see 3.3.1.1.)

Procedure:

1) Inhibition of the endogeneous peroxidase (see 3.3.1.2.)

2) Rinse for 5 min in TBS

3) Insert slides in Shandon Racks

4) Blocking serum for 10 min at room temperature, dilute horse serum 1:5 in TBS 20 min

5) Incubate primary antibody over night at 4°C in the refrigerator

Dilute the antibody in TBS (see 3.3.1.4.)

6) Rinse 3 x 5 min in TBS buffer

7) Incubate the secondary antibody for 30 min at room temperature, Biotinylated Horse anti-Mouse IgG (H+L)

Preparation: 9 µl for 1 ml TBS buffer

8) Rinse the sections 3 x 5 min in TBS buffer

9) Incubate the ABC complex for 30 min at room temperature

Preparation: 9 µl Avidin + 9 µl Biotin for 1 ml TBS buffer

Attention! It has to be prepared 30 min before use

10) Then as above (see 3.3.1.5.)

3.3.2.5. Neurofilament

Antibody: Mouse anti-neurofilament (clone 2F11)

Provenance: Dako Cytomation GmbH, Hamburg

Sections: Deparaffinized sections (see 3.3.1.1.)

Procedure:

1) Inhibition of the endogeneous peroxidase (see 3.3.1.2.)

2) Rinse for 5 min in TBS

3) Insert slides in Shandon Racks

4) Blocking serum for 10 min at room temperature, horse serum.

Incubate primary antibody over night at 4°C in the refrigerator.

Dilute the antibody in TBS with 1 % BSA (see 3.3.1.4.)

5) Rinse 3 x 5 min in TBS buffer

6) Incubate the secondary antibody for 30 min at room temperature, Biotinylated Horse anti-Mouse IgG (H+L)

Preparation: 9 µl for 1 ml TBS buffer

7) Rinse the sections 3 x 5 min in TBS buffer

8) Incubate the ABC complex for 30 min at room temperature

Preparation: 9 µl Avidin + 9 µl Biotin for 1 ml TBS buffer

Attention! It has to be prepared 30 min before use

9) Then as above (see 3.3.1.5.)

3.3.2.6. Glial fibrillary acidic protein (GFAP)

Antibody: Rabbit anti-GFAP (rabbit polyclonal)

Provenance: Dako Cytomation GmbH, Hamburg

Sections: Deparaffinized sections (see 3.3.1.1.)

Procedure:

1) Inhibition of the endogeneous peroxidase (see 3.3.1.2.)

2) Rinse for 5 min in TBS

3) Insert slides in Shandon Racks

4) Blocking serum for 10 min at room temperature, swine serum

Incubate primary antibody over night at 4°C in the refrigerator

Dilute the antibody in TBS with 20% SS (see 3.3.1.4.)

5) Rinse 3 x 5 min in TBS buffer

6) Incubate the secondary antibody for 30 min at room temperature, Goat anti-Rabbit IgG

Preparation: 9 µl for 1 ml TBS with 20% SS

7) Rinse the sections 3 x 5 min in TBS buffer

8) Incubate the ABC complex for 30 min at room temperature

Preparation: 9 µl A+ 9 µl B dilute 1 ml TBS

9) Then as above (see 3.3.1.5.)

3.3.2.7. Melan A

Antibody: Mouse anti-melan A (clone A103)

Provenance: Dako Cytomation GmbH, Hamburg

Sections: Deparaffinized sections (see 3.3.1.1.)

Procedure:

1) Inhibition of the endogeneous peroxidase (see 3.3.1.2.)

2) Rinse for 5 min in TBS

3) Pre-processing with citrate (see 3.3.1.3.2.)

4) Insert slides in Shandon Racks

5) Blocking serum for 10 min at room temperature, horse serum

Incubate primary antibody over night at 4°C in the refrigerator

Dilute the antibody in TBS with 1 % BSA (see 3.3.1.4.)

6) Rinse 3 x 5 min in TBS buffer

7) Incubate the secondary antibody for 30 min at room temperature, Biotinylated Horse anti-Mouse IgG (H+L)

Preparation: 9 µl for 1 ml TBS buffer

8) Rinse the sections 3 x 5 min in TBS buffer

9) Incubate the ABC complex for 30 min at room temperature

Preparation: 9 µl Avidin + 9 µl Biotin for 1 ml TBS buffer

Attention! It has to be prepared 30 min before use

10) Then as above (see 3.3.1.5.)

3.3.2.8. Factor VIII

Antibody: Rabbit anti-factor VIII (rabbit polyclonal)

Provenance: Dako Cytomation GmbH, Hamburg

Sections: Deparaffinized sections (see 3.3.1.1.)

Procedure:

1) Inhibition of the endogeneous peroxidase (see 3.3.1.2.)

2) Rinse for 5 min in TBS

3) Pre-processing with Protease (see 3.3.1.3.1.)

4) Insert slides in Shandon Racks

5) Blocking serum for 10 min at room temperature, swine serum

Incubate primary antibody over night at 4°C in the refrigerator.

Dilute the antibody in TBS with 20% SS (see 3.3.1.4.)

6) Rinse 3 x 5 min in TBS buffer

7) Incubate the secondary antibody for 30 min at room temperature, Biotinylated Goat anti-Rabbit IgG

Preparation: 9 µl for 1 ml TBS with 20% SS

8) Rinse the sections 3 x 5 min in TBS buffer

9) Incubate the ABC complex for 30 min at room temperature

Preparation: 9 µl A + 9 µl B dilute 1 ml TBS

10) Then as above (see 3.3.1.5.)

3.3.2.9. MHC II

Antibody: Mouse anti-human HLA-DR, alpha chain (clone TAL.1B5)

Provenance: Dako Cytomation GmbH, Hamburg

Sections: Deparaffinized sections (see 3.3.1.1.)

Procedure:

1) Inhibition of the endogeneous peroxidase (see 3.3.1.2.)

2) Rinse for 5 min in TBS

3) Pre-processing with citrate (see 3.3.1.3.2.)

4) Insert slides in Shandon Racks

5) Blocking serum for 10 min at room temperature, rat serum 10% in TBS

Incubate primary antibody over night at 4°C in the refrigerator

Dilute the antibody in TBS (see 3.3.1.4.)

6) Rinse 3 x 5 min in TBS buffer

7) Incubate the secondary antibody for 30 min at room temperature, Rat anti-Mouse IgG

Preparation: dilute 1:1000 in TBS

8) Rinse the sections 3 x 5 min in TBS buffer

9) Incubate the mouse PAP complex for 30 min at room temperature

Preparation: dilute 1:500 in TBS

10) Then as above (see 3.3.1.5.)

3.3.2.10. Lysozyme

Antibody: Rabbit anti-lysozyme (rabbit polyclonal)

Provenance: Dako Cytomation GmbH, Hamburg

Sections: Deparaffinized sections (see 3.3.1.1.)

Procedure:

1) Inhibition of the endogeneous peroxidase (see 3.3.1.2.)

2) Rinse for 5 min in TBS

3) Pre-processing with Protease (see 3.3.1.3.1.)

4) Insert slides in Shandon Racks

5) Blocking serum not applied

Incubate primary antibody over night at 4°C in the refrigerator

Dilute the antibody in TBS/5 % dog serum (see 3.3.1.4.)

6) Rinse 3 x 5 min in TBS buffer

7) Incubate the secondary antibody for 30 min at room temperature, swine anti-rabbit IgG

Preparation: dilute 1:100 in TBS with 5 % dog serum

8) Rinse the sections 3 x 5 min in TBS buffer

9) Incubate the PAP from rabbit for 30 min at room temperature

Preparation: dilute 1:100 in TBS with 5 % dog serum

10) Then as above (see 3.3.1.5.)

3.3.2.11. CD3

Antibody: Rabbit anti-CD3 (clone pAb)

Provenance: Dako Cytomation GmbH, Hamburg

Sections: Deparaffinized sections (see 3.3.1.1.)

Procedure:

1) Inhibition of the endogeneous peroxidase (see 3.3.1.2.)

2) Rinse for 5 min in TBS

3) Pre-processing with Protease (see 3.3.1.3.1.)

4) Insert slides in Shandon Racks

5) Blocking serum for 15 min at room temperature, dilute swine serum 1:5 in TBS

Incubate primary antibody over night at 4°C in the refrigerator

Dilute the antibody in TBS/20 % SS (see 3.3.1.4.)

6) Rinse 3 x 5 min in TBS buffer

7) Incubate the secondary antibody for 30 min at room temperature, Biotinylated Goat anti-Rabbit IgG (H+L)

Preparation: 9 µl for 1 ml TBS buffer / 20 % SS

8) Rinse the sections 3 x 5 min in TBS buffer

9) Incubate the ABC complex for 30 min at room temperature

Preparation: 9 µl Avidin + 9 µl Biotin for 1 ml TBS buffer

Attention! It has to be prepared 30 min before use

10) Then as above (see 3.3.1.5.)

3.3.2.12. CD45R

Antibody: CD45R (clone B220 (Ly 5))

Provenance: Linaris GmbH, Bettingen Stadt Wertheim

Sections: Deparaffinized sections from cat (see 3.3.1.1.)

Procedure:

1) Inhibition of the endogeneous peroxidase (see 3.3.1.2.):

2) Rinse for 5 min in TBS

3) Pre-processing with citrate (see 3.3.1.3.2.)

4) Insert slides in Shandon Racks

5) Blocking serum for 10 min at room temperature, horse serum

Incubate primary antibody over night at 4°C in the refrigerator

Dilute the antibody in TBS with 1 % BSA (see 3.3.1.4.)

6) Rinse 3 x 5 min in TBS buffer

7) Incubate the secondary antibody for 30 min at room temperature, Biotinylated Rabbit anti-Rat IgG (H+L)

Preparation: 9 µl for 1 ml TBS buffer

8) Rinse the sections 3 x 5 min in TBS buffer

9) Incubate the ABC complex for 30 min at room temperature

Preparation: 9 µl Avidin + 9 µl Biotin for 1 ml TBS buffer

Attention! It has to be prepared 30 min before use

10) Then as above (see 3.3.1.5.)

3.3.2.13. CD79α

Antibody: Mouse anti-B-cell CD79αcy (clone HM57)

Provenance: Dako Cytomation GmbH, Hamburg

Sections: Deparaffinized sections from cat (see 3.3.1.1.)

Procedure:

1) Inhibition of the endogeneous peroxidase (see 3.3.1.2.)

2) Rinse for 5 min in TBS

3) Pre-processing with citrate (see 3.3.1.3.2.)

4) Insert slides in Shandon Racks

5) Blocking serum for 10 min at room temperature, horse serum

Incubate primary antibody over night at 4°C in the refrigerator

Dilute the antibody in TBS with 1 % BSA (see 3.3.1.4.)

6) Rinse 3 x 5 min in TBS buffer

7) Incubate the secondary antibody for 30 min at room temperature, Biotinylated Horse anti-Mouse IgG (H+L)

Preparation: 9 µl for 1 ml TBS buffer

8) Rinse the sections 3 x 5 min in TBS buffer

9) Incubate the ABC complex for 30 min at room temperature

Preparation: 9 µl Avidin + 9 µl Biotin for 1 ml TBS buffer

Attention! It has to be prepared 30 min before use

10) Then as above (see 3.3.1.5.)

3.3.2.14. Neuron Specific Enolase (NSE)

Antibody: Anti-NSE (monoclonal antibody)

Provenance: “Zymed” Invitrogen GmbH, Karlsruhe

Sections: Deparaffinized sections (see 3.3.1.1.)

Procedure:

1) Inhibition of the endogeneous peroxidase (see 3.3.1.2.)

2) Rinse for 5 min in TBS

3) Pre-processing with citrate (see 3.3.1.3.2.)

4) Insert slides in Shandon Racks

5) Blocking serum for 10 min at room temperature, horse serum

Incubate primary antibody over night at 4°C in the refrigerator

Dilute the antibody in TBS with 1 % BSA (see 3.3.1.4.)

6) Rinse 3 x 5 min in TBS buffer

7) Incubate the secondary antibody for 30 min at room temperature, Biotinylated Horse anti-Mouse IgG (H+L)

Preparation: 9 µl for 1 ml TBS buffer

8) Rinse the sections 3 x 5 min in TBS buffer

9) Incubate the ABC complex for 30 min at room temperature

Preparation: 9 µl Avidin + 9 µl Biotin for 1 ml TBS buffer

Attention! It has to be prepared 30 min before use

10) Then as above (see 3.3.1.5.)

3.3.2.15. Synaptophysin

Antibody: Anti-synaptophysin (clone SY38)

Provenance: Dako Cytomation GmbH, Hamburg

Sections: Deparaffinized sections (see 3.3.1.1.)

Procedure:

1) Inhibition of the endogeneous peroxidase (see 3.3.1.2.)

2) Rinse for 5 min in TBS

3) Pre-processing with citrate (see 3.3.1.3.2.)

4) Insert slides in Shandon Racks

5) Blocking serum for 10 min at room temperature, horse serum

Incubate primary antibody over night at 4°C in the refrigerator

Dilute the antibody in TBS with 1 % BSA (see 3.3.1.4.)

6) Rinse 3 x 5 min in TBS buffer

7) Incubate the secondary antibody for 30 min at room temperature, Biotinylated Horse anti-Mouse IgG (H+L)

Preparation: 9 µl for 1 ml TBS buffer

8) Rinse the sections 3 x 5 min in TBS buffer

9) Incubate the ABC complex for 30 min at room temperature

Preparation: 9 µl Avidin + 9 µl Biotin for 1 ml TBS buffer

Attention! It has to be prepared 30 min before use

10) Then as above (see 3.3.1.5.)

3.3.2.16. S100

Antibody: Anti-S100 (rabbit polyclonal)

Provenance: Dako Cytomation GmbH, Hamburg

Sections: Deparaffinized sections (see 3.3.1.1.)

Procedure:

1) Inhibition of the endogeneous peroxidase (see 3.3.1.2.)

2) Rinse for 5 min in TBS

3) Insert slides in Shandon Racks

4) Blocking serum for 30 min at room temperature, dilute swine serum 1:5 in TBS

Incubate primary antibody over night at 4°C in the refrigerator

Dilute the antibody in TBS (see 3.3.1.4.)

5) Rinse 3 x 5 min in TBS buffer

6) Incubate the secondary antibody for 30 min at room temperature, Swine anti-Rabbit IgG

Preparation: 9 µl for 1 ml TBS buffer

7) Rinse the sections 3 x 5 min in TBS buffer

8) Incubate the ABC complex for 30 min at room temperature

Preparation: 9 µl Avidin + 9 µl Biotin for 1 ml TBS buffer

Attention! It has to be prepared 30 min before use

9) Then as above (see 3.3.1.5.)

3.3.2.17. MAC387

Antibody: Anti-Myeloid/Histocyte Antigen (clone MAC387)

Provenance: Dako Cytomation GmbH, Hamburg

Sections: Deparaffinized sections (see 3.3.1.1.)

Procedure:

1) Inhibition of the endogeneous peroxidase (see 3.3.1.2.)

2) Rinse for 5 min in TBS

3) Pre-processing with Protease (see 3.3.1.3.1.)

4) Insert slides in Shandon Racks

5) Blocking serum for 30 min at room temperature, rat serum 1:10 dilute in TBS

Incubate primary antibody over night at 4°C in the refrigerator

Dilute the antibody in TBS (see 3.3.1.4.)

6) Rinse 3 x 5 min in TBS buffer

7) Incubate the secondary antibody for 30 min at room temperature, Swine anti-Rabbit IgG

Preparation: 9 µl for 1 ml TBS buffer

8) Rinse the sections 3 x 5 min in TBS buffer

9) Incubate the ABC complex for 30 min at room temperature

Preparation: 9 µl Avidin + 9 µl Biotin for 1 ml TBS buffer

Attention! It has to be prepared 30 min before use

10) Then as above (see 3.3.1.5.)

3.3.2.18. Smooth muscle actin

Antibody: Mouse anti-smooth muscle actin (clone 1A4)

Provenance: Dako Cytomation GmbH, Hamburg

Sections: Deparaffinized sections (see 3.3.1.1.)

Procedure:

1) Inhibition of the endogeneous peroxidase (see 3.3.1.2.)

2) Rinse for 5 min in TBS

3) Pre-processing with citrate (see 3.3.1.3.2.)

4) Insert slides in Shandon Racks

5) Blocking serum for 10 min at room temperature, horse serum

Incubate primary antibody over night at 4°C in the refrigerator

Dilute the antibody in TBS with 1 % SS (see 3.3.1.4.)

6) Rinse 3 x 5 min in TBS buffer

7) Incubate the secondary antibody for 30 min at room temperature, Biotinylated Horse anti-Mouse IgG (H+L)

Preparation: 9 µl for 1 ml TBS buffer

8) Rinse the sections 3 x 5 min in TBS buffer

9) Incubate the ABC complex for 30 min at room temperature

Preparation: 9 µl Avidin + 9 µl Biotin for 1 ml TBS buffer

Attention! It has to be prepared 30 min before use

10) Then as above (see 3.3.1.5.)

4. RESULTS

4.1. Tumors in dogs

In this part, we will expose 816 skin tumors and tumor-like lesions of 768 dogs in different aspects as follows.

4.1.1. Sex distribution

For 7 dogs out of 768 dogs, the sex was not stated, and the remainder was distributed as in table 4.

Tab. 4: Sex distribution (n=761)

Sex	*Castrated*	*Non castrated*	*Total*	*%*
♂	45	384	429	56.4
♀	48	284	332	43.6
Total	93	668	761	100.0

4.1.2. Anatomical location

For 13 out of 816 canine skin tumors and tumor-like lesions, there were no data regarding their location, the remainder are described in table 5.

Tab. 5: The distribution of canine tumors and tumor-like lesions of the skin (n=803)

Location	No. of tumors	%
Limb	279	34.7
Head	191	23.8
Perianal	77	9.6
Chest	66	8.2
Neck	63	7.8
Back	54	6.7
Abdominal	45	5.6
Mammary region	17	2.1
Tail	8	1.0
Whole body	3	0.4
Total	803	100.0

4.1.3. Breed disposition

Data regarding breed were reported in 745 cases, involving 109 different dog breeds in this collection.

Mongrels were the most common dogs followed by other breeds as in table 6.

Tab. 6: Breed disposition

Breed	No	%
Mongrel	192	25.8
German shepherd dog	54	7.2
Boxer	33	4.4
Golden retriever	30	4.0
Westhighland white terrier	27	3.6
Cocker spaniel	26	3.5
Bernese mountain dog	25	3.4
Rottweiler	20	2.7
Roughhaired dachshund	19	2.6
Dobermann	19	2.6
Poodle	17	2.3
Labrador	16	2.1
Dachshund	11	1.5
Muensterlaender	11	1.5
Standard schnauzer	11	1.5
Yorkshire terrier	9	1.2
Pitbull	9	1.2
Hovawart	8	1.1
Giant schnauzer	8	1.1
Airedale terrier	8	1.1
Jack russel terrier	8	1.1

Breed	No	%
Bobtail	7	0.9
Husky	7	0.9
Staffordshire terrier	7	0.9
German wirehaired pointer	6	0.8
Newfoundland	6	0.8
Setter	6	0.8
Terrier (breed not further specified)	6	0.8
Beagle	5	0.7
Longhair dachshund	5	0.7
Irish setter	5	0.7
Scotch terrier	5	0.7
Bernhardiner	4	0.5
Border colli	4	0.5
Collie	4	0.5
Dalmatin	4	0.5
German shorthaired pointer	4	0.5
Schnauzer (breed not further specified)	4	0.5
Gordon setter	4	0.5
Shi-tzu	3	0.4
American staffordshire terrier	3	0.4

The following 17 dog breeds showed two cases (0.3 %) for each: Bouvier, Bordeaux dog, Bulldog, Siberian husky, Kuvasz, Small munsterlander, Pekinese, Pinscher, Retriever, Canadian shepherd dog, Springer spaniel, Terrier (breed not further specified), Fox terrier, Hunting terrier, Kerry blue terrier, Tibetan terrier and Wachtel dog.

The following 51 dog breeds showed only one case (0.1 %) for each: Afghan, Akita, Appenzeller, Basset, Bayrischer Gebirgsschweisshund, Berger de brie, Bracke, Schwarzwaldbracke, Briard, Chihuahua, Chow-chow, Bearded collie, Dogge, American bulldog, German dogge, French bulldog, Tibet dogge, Epagneul, Eurasier, Hannoverscher Schweisshund, Huetehund, Altdeutscher huetehund, Lahaso apso, Leonberger, Malamute, Maltese dog, Mastiff, Large munsterlaender, Otterhund, Pastor majorkin, Miniature pinscher, Pon, Poodle, Pointer, Large poodle, Miniature poodle, Jagd retriever, Samojede, American shepherd dog, Canadian shepherd, Australian shepherd, Belgian shepherd, Miniature schnauzer, English setter, Bedlington terrier, Cairn terrier, Softcoated wheaten terrier, Staffordshire bull terrier, Welsh terrier, Weimaraner, Irish wolfhound, Wolfshound and Wolfsspitz.

4.1.4. Age distribution

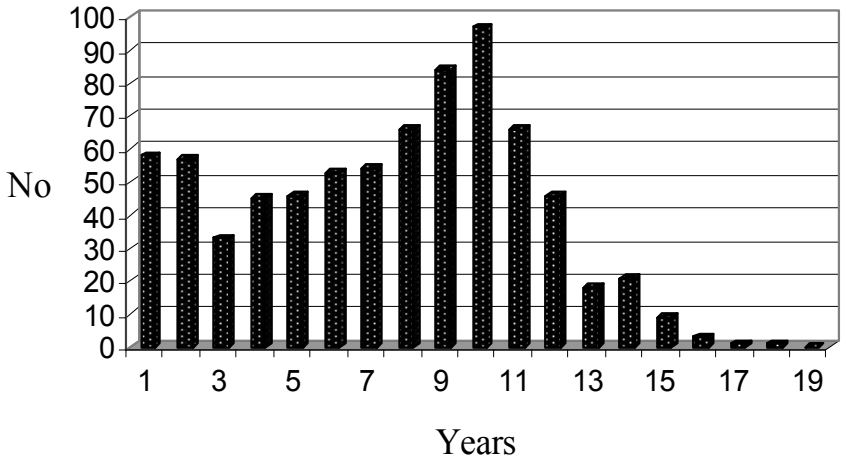
10 cases out of 768 cases were of unknown age; the remainder 758 was distributed as in table 7.

Tab. 7: Age distribution of dogs (n=758)

Age in years	Number of cases	%
to 1 year	58	7.7
2	57	7.5
3	33	4.4
4	45	5.9
5	46	6.1
6	53	7.0
7	54	7.1
8	66	8.7
9	84	11.1
10	97	12.8

Age in years	Number of cases	%
11	66	8.7
12	46	6.1
13	18	2.4
14	21	2.8
15	9	1.2
16	3	0.4
17	1	0.1
18	1	0.1
19	0	0.0
Total	758	100.0

Diag. 3: Age distribution in years (n=758).



4.1.5. Origin of tumors and tumor-like lesions

Epithelial, mesenchymal and melanocytic origins are the three main groups close to the WHO classification, and tumor-like lesions were distributed among these groups and the results are represented in diagram 4.

Diag. 4: Origin of tumors and tumor-like lesions (n=816)

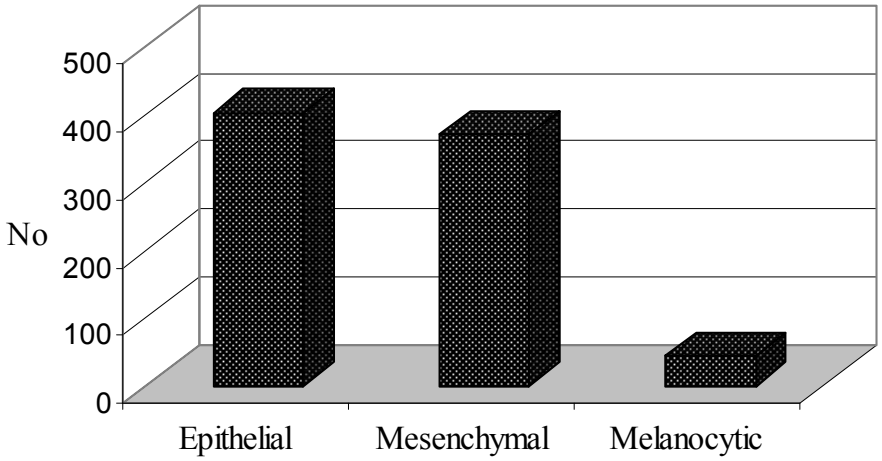


Diagram 4 shows three tumor groups, 403 tumors (49.3 %) of epithelial, 370 tumors (45.3 %) of mesenchymal and 43 tumors (5.3 %) of melanocytic origin.

4.1.6. Prevalence of individual groups of skin tumors

816 skin tumors and tumor-like lesions are divided into groups according to the new WHO classification, as in the table 8.

There are three tumor groups for which there are no cases, and these are tumors metastatic to the skin, tumors of striated muscle and tumors of mesothelium.

Tab. 8: Prevalence of individual groups of skin tumors (n=816)

Tumor	*Number of tumors*	*%*
Tumors with adnexal differentiation	217	26.6
Histiocytic tumors	141	17.3
Cysts	85	10.4
Tumors of fibrous tissue	63	7.7
Mast cell tumors	56	6.9
Tumor-like lesions	51	6.3
Tumors of adipose tissue	46	5.6
Melanocytic tumors	43	5.3
Tumors of vascular tissue	26	3.2
Tumors of the epidermis	24	2.9
Hamartomas	22	2.6
Unclassified tumors	19	2.3
Miscellaneous tumors	13	1.6
Epithelial tumors without sqamous or adnexal differentiation	5	0.6
Tumors of synovium	2	0.2
Tumors of peripheral nerves	2	0.2
Tumors of smooth muscle	1	0.1

4.1.7. Prevalence of individual types of skin tumors

110 types represent the skin tumors and tumor-like lesions in all animal species according to the new WHO classification, 54 types are listed in table 9, in descending order as to numbers and percentages of the tumors.

8 types were represented only by one case (0.1 %) each, and they were apocrine hamartoma, complex and mixed apocrine carcinoma, hepatoid gland carcinoma, leiomyosarcoma, malignant trichoepithelioma, multicentric squamous cell carcinoma in situ, myxoma, and pressure point comedones.

Many of the skin tumors were specific for some animal species, and many were not reported or are rare in dogs. However, the tumors that were not found in the dogs of our collection were anal sac gland adenoma, angiolipoma, basal cell carcinoma, benign peripheral nerve sheath tumor of skin and subcutis, ceruminous adenoma, ceruminous gland carcinoma, complex and mixed ceruminous carcinoma, complex and mixed ceruminous adenoma, eccrine adenoma, eccrine carcinoma, granular cell tumor, inverted papilloma, Kaposi-like vascular tumor, leiomyoma, liposarcoma, lymphangiosarcoma, malignant fibrous histiocytoma, malignant mesenchymoma, malignant pilomatricoma, meibomian ductal adenoma, melanoacanthoma, mesothelioma, rhabdomyoma, rhabdomyosarcoma, sebaceous ductal adenoma, systemic histiocytosis and tricholemmoma. The tumor-like lesions that were not found in the dogs of our collection were traumatic neuroma, scrotal vascular hamartoma, nodular dermatofibrosis of the German shepherd dog, nodular fasciitis, melanocytic hyperplasia, epidermal hamartoma, cutaneous horn, dilated pore, ciliated cyst, warty dyskeratoma and xanthoma.

Some other tumors were found in the skin and subcutaneous tissue in our collection, but were not considered in our collection because they are not classified under skin and soft tissue tumors in the new WHO classification. These were 8 lymphosarcoma, 5 extramedullary plasmocytoma, 4 which could not be classified, three meibomian gland hyperplasias, two chondrosarcomas, and one of each osteosarcoma, hepatoid gland hyperplasia and anal sac gland hyperplasia.

Tab. 9: Prevalence of 54 types of skin and soft tissue tumors and tumor-like lesions.

Tumor	*n*	*%*
Canine cutaneous histiocytoma	134	16.4
Mast cell	56	6.9
Lipoma	46	5.6
Hepatoid gland adenoma	44	5.4
Infundibular cyst	37	4.5
Fibrosarcoma	32	3.9
Sebaceous hyperplasia	23	2.8
Malignant melanoma	22	2.7
Trichoepithelioma	22	2.7
Melanocytoma	21	2.6
Meibomian adenoma	20	2.5
Canine hemangiopericytoma	19	2.3
Hemangioma	19	2.3
Infundibular keratinizing acanthoma	19	2.3
Apocrine cyst	18	2.2
Sebaceous adenoma	17	2.1
Subungual squamous cell carcinoma	17	2.1
Trichoblastoma	16	2.0
Pilomatricoma	14	1.7
Calcinosis circumscripta	13	1.6
Collagenous hamartoma	13	1.6
Fibroma	11	1.3
Fibropruritic nodule	11	1.3
Panfollicular cyst	10	1.2
Sebaceous duct cyst	10	1.2
Follicular hamartoma	9	1.1
Basosquamous carcinoma	8	1.0
Fibroepithelial “polyp”	8	1.0

Tumor	*n*	*%*
Papilloma	8	1.0
Squamous papilloma	8	1.0
Fibroadnexal hamartoma	8	1.0
Apocrine ductal adenoma	7	0.9
Hemangiosarcoma	7	0.9
Squamous cell carcinoma	7	0.9
Anal sac gland carcinoma	5	0.6
Apocrine adenoma	5	0.6
Apocrine carcinoma	5	0.6
Basal cell tumor	5	0.6
Hepatoid gland epithelioma	5	0.6
Myxosarcoma	5	0.6
Sebaceous epithelioma	5	0.6
Dermoid cyst	4	0.5
Isthmus cyst	4	0.5
Malignant histiocytosis	4	0.5
Sebaceous hamartoma	4	0.5
Complex and mixed apocrine adenoma	3	0.4
Cutaneous histiocytosis	3	0.4
Apocrine ductal carcinoma	2	0.2
Malignant peripheral nerve sheath tumor of the skin and subcutis	2	0.2
Meibomian carcinoma	2	0.2
Meibomian epithelioma	2	0.2
Myxoma	2	0.2
Sebaceous carcinoma	2	0.2
Subungual epithelial inclusion cyst	2	0.2
Subungual keratoacanthoma	2	0.2
Synovial cell sarcoma	2	0.2

4.1.8. Entities of skin tumors and tumor-like lesions

4.1.8.1. Basal cell tumor (basal cell epithelioma)

We collected five cases (0.6 %), 4 from males (80%) and one from a female (20%) aged 7, 8, 10, 11 and 12 years, with a mean age of 9.6 years. The tumors were located as follows: two at the limbs and one in each, head and perianal, and one tumor was without data of location. 4 tumors showed cystic degeneration and only one was pure solid. The races of these dogs were two Roughhaired dachshunds, one Poodle, one Airedale terrier and one Mongrel.

The case of perianal tumor had an association with the overlying epidermis, and showed cystic degeneration. This tumor was mixed in one area with hyperplastic hepatoid gland.

4.1.8.2. Follicular tumors

These were 72 tumors and they had been diagnosed as in the table 10.

Tab. 10: Follicular tumors (n=72)

Follicular tumor	*n*	*%*	♂ %	♀ %	*Location*	*Breed*	*Age in years (mean)*
Infundibular keratinizing acanthoma	19	26	58	42	5 back, 4 limb, 3 neck, 2 each head and perianal, and 1 each chest and tail*	8 Mongrels, 4 German shepherd dogs, 2 Collies, 1 of each Bayrischer gebirgsschweisshund, Berger de brie, Hovawart, Golden Retriever and Wachtel	8*
Tricholemmoma	0	0					
Trichoblastoma	16	22	69	31	9 head, 2 neck, 2 limbs and 1 perianal**	4 Mongrels, 2 German shepherd dogs, 2 Westhighland white terriers, and one for each Hovawart, Epagneul, Muensterlaender, Poodle, English Setter, Irish Setter, Terrier and Yorkshire Terrier.	8**
Trichoepithelioma	22	31	50	50	7 back, 5 chest, 2 limb one of each head, neck, perianal and tail***	6 Mongrels, 6 German shepherd dogs, 2 Muensterlaenders and one of each Bernese mountain dog, Bordercollie, German shorthaired pointer, Otterhund, Poodle, Setter, Cocker spaniel***	8
Malignant trichoepithelioma	1	1	100	0	unknown	Westhighland white terrier	11
Pilomatricoma	14	19	36	64	4 back, 4 limb, 2 of each abdomen and perianal and one head****	3 Mongrels, 3 Airedale terriers, 2 Jack Russel Terriers, and one of each Bobtail, Tibet dogge, Large poodle, Giant schnauzer and Shi-tzu****	6
Malignant pilomatricoma	0	0					
Total	**72**	100					

* One without location data and one without age data. , ** One without age data and two without location data., *** 4 without location data and one without breed data.
**** One without location data and one without breed data.

4.1.8.2.1. Trichoblastomas

Because of the significance of trichoblastomas in our study, we demonstrate these tumors in detail.

15 dogs were aged between one and 14 years, with a mean age of 8 years. Three cases were observed in animals at an age of 6 years, two at 10 and 12 years and one case of 1, 2, 4, 5, 8, 11, 13 and 14 years, respectively.

Trabecular type was not found, and one mixed form of ribbon with granular cell type was found. The cells in two ribbon trichoblastomas showed clear cytoplasm, 4 ribbon trichoblastomas were medusoid, 4 were mixed ribbon and medusoid, one was mixed with spindle cell type, and the other 4 tumors were pure ribbon type (Table 11).

Tab. 11: Trichoblastoma types (n=16)

Tumor variant	*n*	*%*
Ribbon*	14	88
Spindle	1	6
Granular	1	6
Trabecular	0	0

*The ribbon type includes medusoid type.

For two tumors there were no data regarding location, the other 14 tumors were distributed as in table 12.

Tab. 12: Trichoblastoma, locations (n=14)

Location	*n*	*%*
Head	9	64
Neck	2	14
Limbs	2	14
Perianal	1	7

The case of granular cell trichoblastoma was found in the auricle of a 10-year old male Epagneul dog. Histologically, two distinct types of neoplastic epithelium were present, basaloid and granular cells. Usually, the basaloid cells are arranged in ribbons and clusters embedded in a moderate amount of fibrovascular stroma. These cells were typical of those seen in ribbon-type trichoblastomas. The granular cells were arranged in clusters of uniform appearance, closely packed, and somewhat polygonal. Nuclei often were eccentric and were more angular than those of the trichoblastoma. Very few mitoses were present, but less frequently than in the trichoblastoma. The cytoplasm was plentiful and slightly eosinophilic with a fine granular appearance. The fine cytoplasmic granules were moderately PAS positive

and did not express with vimentin, lysozyme and S100, however, the cells expressed cytokeratin.

4.1.8.2.1.1. Clear cell trichoblastomas

Two cases of trichoblastomas were diagnosed in young dogs and were described as follows:
A hazelnut-sized tumor of the mandiblular region was found in a 2-year-old, intact, female Westhighland white terrier. The other tumor was almond-sized and found between the toes of a 1-year-old, intact, male Mongrel dog. They were exophytic and non-ulcerated skin nodules, with a lobular white cut surface.
Both tumors consisted of epithelial cells mostly of moderate size and uniform appearance but some scattered cells were of large size. About 30% to 40% of the tumor cells in both cases were basaloid and arranged in ribbons, clusters and islands. However, the predominating tumor cells had pale, sometimes vacuolated cytoplasm and possessed a central, ovoid to round, sometimes hyperchromatic, but mostly hypochromatic nucleus and showed growth patterns is of either a solid mass, cords or sometimes nests of cells. The tumor cells showed a moderate mitotic rate. A few scattered large cells that had abundant cytoplasmic vacuoles which indented the nuclei were present in both cases and were consistent with sebaceous differentiation. In one of these tumors, the tumor cells were close to the base of a hair follicle. The cells showed significant amounts of PAS-positive cytoplasmic granules which were not resistant to diastase and considered to be glycogen. The same granules were also present in the normal cells of the lower part of external root sheath of the hair follicles in the same slides. Additionally, some clear cells were arranged in islands that sometimes were surrounded by an eosinophilic, acellular, vitreous sheath which stained positively with periodic acid-Schiff (PAS) and blue with Masson's trichrome stains. Furthermore, some islands showed few central cells that had eosinophilic cytoplasm.

4.1.8.3. Cysts

Generally, 85 skin cysts were found in 83 dogs, of which 46 (55 %) were females and 37 (45 %) were males. The dogs were 17 (21 %) Mongrels, 8 (10%) Boxer, 6 (7 %) Westhighland white terrier, 5 (6 %) German shepherd dog, 4 (5 %) each Dobermann and Cocker spaniel, three (4 %) each Bobtail, Pit bull terrier, Poodle and Golden retriever, two (2 %) each Bernese mountain dog, Labrador and Munsterlaender (breed not further specified) and Gordon setter, one (1 %) each Bouvier, Bracke, Chow-chow, Collie, Dachshund, Roughhaired dachshund, German wirehaired pointer, Hovawart, Newfoundland, Miniature pinscher, Miniature poodle,

Rottweiler, Standard schnauzer, Giant schnauzer, Bull terrier, Jack russel terrier and Staffordshire terrier. For two dogs there were no data regarding their breed.

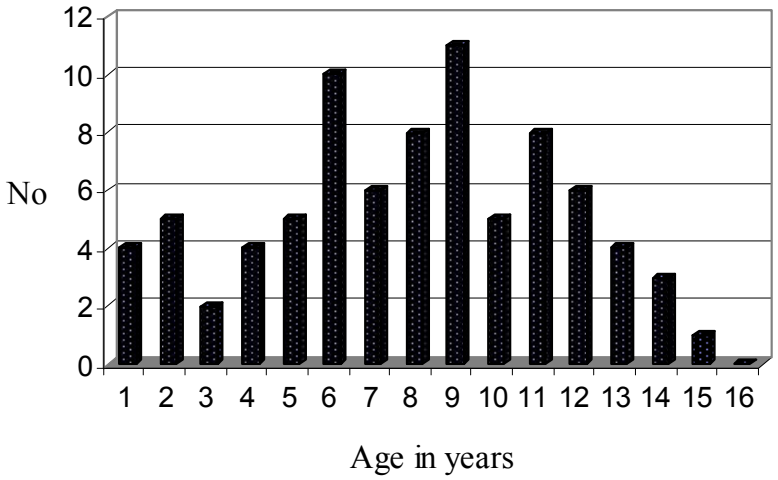
For 6 skin cysts, there were no data on location, the other 79 are reported in table 13.

Tab. 13: Skin cysts, locations (n=79)

Location	*n. of cysts*	*%*
Limb	24	30
Head	20	25
Neck	8	10
Mammary region	7	9
Chest	6	8
Back	6	8
Perianal	4	5
Abdominal	3	4
All body	1	1
Tail	0	0
Total	79	100

82 dogs were divided as in diagram 5, with a mean age of 9 years. For one dog no age was given.

Diag. 5: Skin cysts, age distribution (n=82)



Sex, location, breed, mean age and number of cases of every cyst type of 85 skin cysts are demonstrated in the table 14.

Tab. 14: Skin cysts (n=85)

Cyst	*n*	*%*	♂ *%*	♀ *%*	*Location*	*Breed*	*Age in years (mean)*
Infundibular cyst	37	44	42	58*	8 head, 6 mammary gland region, 6 limbs, 4 back, 2 of each chest, neck, perianal*	5 Mongrel, 4 German shepherd dog, 4 Boxer, 3 Westhighland white terrier, 2 of each Gordon setter, Cocker spaniel, Pitbull, Poodle, Bobtail, and 1 of each Giant schnauzer, Staffordshire terrier, Collie, German wirehaired pointer, Dobermann, Labrador, Muensterlaender, Zwerg pinscher, Zwerg poodle, and Golden retriever*	7
Apocrine cyst	18	21	22	78	5 head, 4 limbs, 3 neck, 2 chest, 2 back, 1 perianal, 1 all the body	6 Mongrel, 3 Westhighland white terrier,1 of each Bernese mountain dog, Bobtail, Chow-chow, Dachshund, Labrador, Muensterlaender, Standard schnauzer, Cocker spaniel, Bull terrier	11**
Panfollicular	10	12	70	30	5 limbs, 2 neck, 2 head, 1 abdomen***	6 Mongrel, 1 of each Bobtail, German shepherd dog, Cocker spaniel***	9
Sebaceous duct cyst	10	12	80	20	5 limbs, 3 head, 1 chest, 1 mammary gland region	2 Boxer, 2 Dobermann, 1 of each Rough-haired dachshund, Hovawart, Mongrel, Newfoundland, Pitbull, Poodle	8
Isthmus cyst	4	5	25	75	2 limbs, 1 of each perianal and chest	Rottweiler, Bernese mountain dog, Bouvier, Jack russel terrier	5
Dermoid cyst	4	5	50	50	3 head and 1 neck	2 Boxer, 2 Golden retriever	4
Subungual epithelial inclusion cyst	2	2	50	50	2 limbs	1 Dobermann, 1 Bracke	8
Dilated pore	0	0	0	0			0
Ciliated cyst	0	0	0	0			0
Total	**85**	100					

* One without sex data, 5 without location data and 1 without breed data. ** One without age data. *** One without location data and one without data concerning breed.

4.1.8.4. Hamartomas

Generally, we collected 22 epithelial and 13 mesenchymal hamartomas. Epithelial hamartomas were found in 22 dogs, 11 (52 %) of which were males and 10 (48 %) females, and for one dog the sex was not stated. These dogs were 10 Mongrels, 2 German shepherd dogs, and one each Saint bernard, Boxer, Briard, Roughhaired dachshund, Dobermann, Pit bull terrier, Golden retriever, Jagd retriever, Rottweiler, and Jack russel terrier.

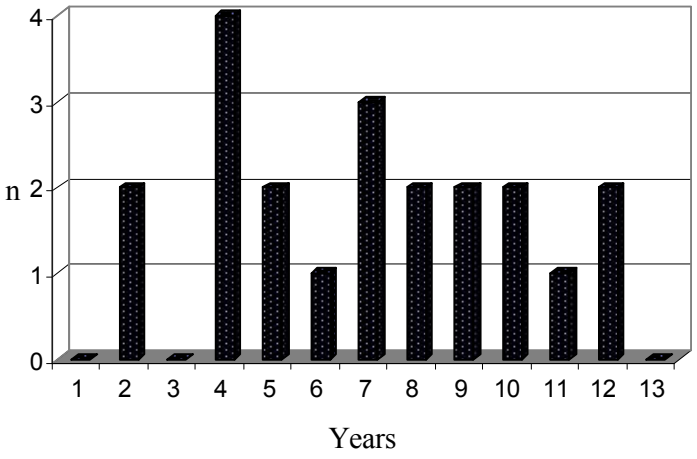
No hamartoma was found at head, mammary region or chest, and for one hamartoma there were no location data. The other 21 hamartomas were distributed as in table 15.

Tab. 15: Hamartomas (n=21)

Location	*n. of cysts*	*%*
Limb	13	62
Neck	3	14
Back	2	10
Perianal	1	5
Abdominal	1	5
Tail	1	5
Total	21	100

The ages of 21 dogs with hamartomas were as shown in diagram 6, and one case was without age data.

Diag. 6: Hamartomas, age distribution (n=21)



Mesenchymal hamartomas in the WHO classification are scrotal vascular hamartoma and collagenous hamartoma; scrotal vascular hamartoma was not found in this collection. The collagenous hamartoma is exposed with the other epithelial types in table 16.

Tab. 16: Hamartomas (n=35)

Hamartoma	*n*	*%*	♂ *%*	♀ *%*	*Location*	*Breed*	*Age in years (mean)*
Apocrine hamartoma	1	3	100	0	neck	Bernhardiner	6
Fibroadnexal hamartoma	8	23	62.5	37.5	5 limbs, 1 of each perianal, neck, tail	4 Mongrel, one of each Boxer, Rough-haired dachshund, Dobermann, Jack russel terrier	6*
Follicular hamartoma	9	26	44	56	6 limbs, 1 back, 1 neck**	4 Mongrel, and one of each Pitbull, Jagd retriever, Rottweiler, German shepherd dog, Briard	7
Sebaceous hamartoma	4	11	33	67***	2 limbs, 1 abdomen, 1 back	2 Mongrel, 1 Golden retriever, 1 German shepherd dog	9
Collagenous hamartoma	13	37	38	62	2 limbs, 2 head, 1 of each neck, chest, back, abdomen****	5 Mongrel, 2 Westhighland white terrier and 1 of each German wirehaired pointer, Dobermann, Husky, Poodle Pointer, German shepherd dog and English setter	8

* One without age data.
** One without location data.
*** One without sex data.
**** 5 without location data.

4.1.8.5. Tumor-like Lesions

Because of the great differences between these lesions, they will be demonstrated separately. Cutaneous horn and warty dyskeratoma were not found in our collection.

4.1.8.5.1. Squamous papilloma

8 lesions were found in 5 females (62.5 %) and three males (37.5 %). 4 lesions were located at limbs, three at the head and one at the neck. These lesions were found in one of the following breeds, namely German shorthaired pointer, Hovawart, Mongrel, Munsterlaender (breed not further specified), German shepherd dog, Canadian shepherd dog, Airedale terrier and Bull terrier. The ages of these dogs varied between one and 12 years, with a mean age of 5 years, and only one was without data regarding age.

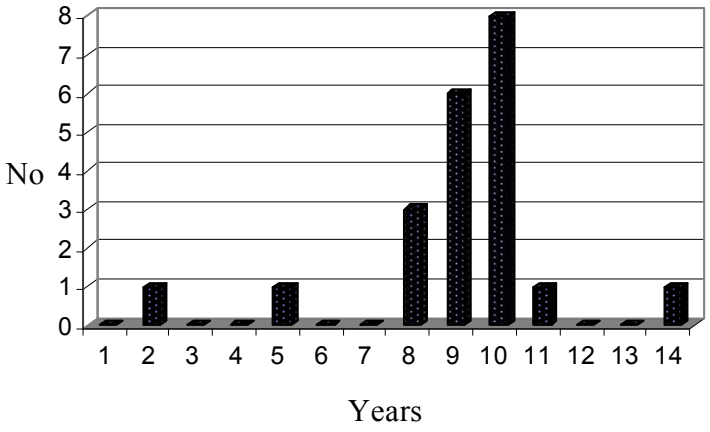
4.1.8.5.2. Pressure point comedones

There was only one pressure point comedone in our collection found at the left elbow of a 14-year-old male Terrier.

4.1.8.5.3. Sebaceous hyperplasia

23 dogs were present in this group, 11 of them were females (52 %), 10 males (48 %) and for two dogs the sex was not stated. The lesions were found as follows: 11 at limbs, 6 head, two back, one of each neck and tail, and two lesions had unknown locations. One dog was without breed data, the other 22 dogs were 5 Mongrels, 4 Poodles, two Labrador retrievers, two Yorkshire terriers, and one of each Boxer, Roughhaired dachshund, Dobermann, Retriever, Cocker spaniel, American staffordshire terrier, Kerry blue terrier, Scotch terrier, and Westhighland white terrier. The dogs were between two and 14-years-old with a mean of 10 years as demonstrated in diagram 7. Two dogs had no age data.

Diag. 7: Age distribution in sebaceous hyperplasia (n=21)



4.1.8.5.4. Fibroepithelial "polyp"

This lesion was found in 6 females (75 %) and two males (25 %), and the dogs were two each of Mongrel, Labrador retriever, Pit bull terrier and the remainder were one Rottweiler and one Husky. 7 lesions were found at different locations as follows: 3 at limbs, two at back, and one at each mammary gland region and neck, and for one lesion there was no data of location. The ages of the animals were from 5 to 18 years, with a mean age of 9 years.

4.1.8.5.5. Fibropruritic nodule

11 cases were found in 7 males (64 %) and 4 females (36 %), 5 of which were found in Mongrels and one each in German wirehaired pointer, Leonberger, Rottweiler, English setter, Cocker spaniel, and Westhighland white terrier. 10 lesions were located as follows: 4 limbs, 3 back, and one each at chest, mammary gland region and tail. One case was of unknown location. The ages of the animals were from two to 12 years, with a mean of 7 years.

4.1.8.6. Tumors of the Epidermis

Inverted papilloma and actinic keratosis were not observed in our collection.

4.1.8.6.1. Papilloma

8 cases were found in 5 males (62.5 %) and three females (37.5 %), 6 of which were located at the head and two at the limbs. This lesion was found in two Mongrels, and one in Dobermann, Hovawart, Golden retriever, Standard schnauzer, Weimaraner and for one dog the breed was not stated. The age of these animals was between two and 6 years, with a mean age of 4 years.

4.1.8.6.2. Multicentric squamous cell carcinoma in situ

Only one instance of this lesion was found at the thigh of a 9-year-old male Airedale terrier.

4.1.8.6.3. Squamous cell carcinoma

6 cases were found in 4 females (67 %) and two males (33 %), 4 of which were located at the head, one was found at each, mammary gland region and neck. This tumor was found one in each German shorthaired pointer, Poodle, Rottweiler, German shepherd dog, Terrier (breed not further specified), and one dog without data of breed. The animals were between 7 to 11-years-old, with a mean of 9 years.

4.1.8.6.4. Basosquamous carcinoma

8 cases were found in 5 males (62.5 %) and three females (37.5 %), two tumors located each at the abdomen and limbs, and one located each at back, chest, head and neck. The tumor was present in two Mongrels and one Saint bernard, Poodle, Rottweiler, Samojede, German shepherd dog, and Cocker spaniel. Animal age was between two and 10 years, with a mean age of 7 years.

4.1.8.7. Nailbed tumors

4.1.8.7.1. Subungual keratoacanthoma

Two tumors were found in one 14-year-old female and one 8-year-old male. Both dogs were Standard schnauzers and the lesions were located at the limbs (Subungual).

4.1.8.7.2. Subungual squamous cell carcinoma

The tumor was found in 18 cases, 11 (61 %) of which were females and 7 (39 %) males. The dogs were 9 Schnauzers (5 Standard schnauzers, two each of Giant schnauzer and Schnauzer {breed not further specified}), two each of Scotch terrier and Mongrel, and one each of Bernese mountain dog, Longhaired dachshund, Labrador retriever, Poodle and Rottweiler. Animal aged between three and 12 years with mean of 9 years.

4.1.8.8. Sebaceous and modified sebaceous gland tumors

These tumors were present in 98 cases; the sebaceous and meibomian ductal adenomas were not found in this collection. The other 9 types are listed in table 17, 18, 19.

The percentages of the three main groups, sebaceous, meibomian and hepatoid were calculated separately.

Tab. 17: Sebaceous tumors (n=24)

Tumor	*n*	*%*	♂ *%*	♀ *%*	*Location*	*Breed*	*Age in years (mean)*
Sebaceous adenoma	17	71	65	35	7 head, 5 limb and one in each mammary gland region neck and perianal*	3 of each Mongrel, Cocker spaniel, 2 Yorkshire terrier and 1 of each Boxer, Dachshund, Husky, Labrador, Muensterlaender, Pekinese, Standard schnauzer, Irish setter, and Westhighland white terrier	9
Sebaceous epithelioma	5	21	100	0	3 head and 2 neck	1 of each Siberian husky, Labrador, Mongrel, Newfoundland and Golden retriever	10
Sebaceous carcinoma	2	8	100	0	one of each head and limb	1 of each Hovawart and Labrador	12

* Two cases without location data.

Tab. 18: Meibomian tumors (n=24)

Tumor	*n*	*%*	♂ *%*	♀ *%*	*Location*	*Breed*	*Age in years (mean)*
Meibomian adenoma	20	83	65	35	20 head (eyelid)	6 Mongrel, 2 of each Irish setter and Cocker spaniel, and 1 of each German wirehaired pointer, Husky, Rottweiler, German shepherd dog, Standard schnauzer, Airedaleterrier, Welsh terrier and Westhighland white terrier*	10
Meibomian epithelioma	2	8	0	100	2 head (eyelid)	One of each Mongrel and Gordon setter	9
Meibomian carcinoma	2	8	100	0	2 head (eyelid)	Golden retriever**	13

* Two cases without breed data. ** One case without breed data.

Tab. 19: Hepatoid gland tumors (n=50)

Tumor	*n*	*%*	♂ *%*	♀ *%*	*Location*	*Breed*	*Age in years (mean)*
Hepatoid gland adenoma	44	88	84	16	41 perianal, 2 abdomen and 1 back	12 Mongrel, 4 Dachshund, 2 of each Husky, Cocker spaniel, Roughhaired dachshund, Westhighland white terrier and one of each Beagle, Bernese mountain dog, Chihuahua, Border collie, Longhair dachshund, Dobermann, Hovawart, Muensterlaender, Pastor Majorkin, Pekinese, Poodle, Schnauzer**, Standard schnauzer, Shi-tzu, Terrier** and Yorkshire terrier*	10
Hepatoid gland epithelioma	5	10	100	0	4 perianal and 1 head	1 of each Husky, Newfoundland, Poodle, German shepherd dog and Springer Spaniel	11
Hepatoid gland carcinoma	1	2	0	100	1 perianal	1 Bernese mountain dog	15

* 4 cases without breed data.

** Breed not further specified

4.1.8.9. Apocrine, modified apocrine gland tumors and eccrine tumors

These lesions were found in 28 dogs. Some types, including ceruminous and eccrine tumors and anal sac gland adenoma, were not found in our collection. The other tumors are listed in table 20.

Tab. 20: Apocrine gland tumors (n=23) and anal sac gland carcinomas (n=5)

Tumor	*n*	*%*	♂ *%*	♀ *%*	*Location*	*Breed*	*Age in years (mean)*
Apocrine adenoma	5	22	80	20	4 neck and 1 limb	2 Mongrel and 1 of each Bernese mountain dog, Bobtail and Dachshund	9
Complex and mixed apocrine adenoma	3	13	67	33	3 limb	One of each Bouvier, German shepherd dog and Giant schnauzer	8
Apocrine ductal adenoma	7	30	29	71	4 head and 1 of each chest, limb and tail	2 Mongrel and 1 of each Bernese mountain dog, Dalmatin, Muensterlaender, Golden retriever and German shepherd dog	10
Apocrine carcinoma	5	22	60	40	1 of each back, limb, head, neck and perianal	1 of each Mongrel, Pitbull, Dalmatin, Kuvasz and Bernhardiner	8
Complex and mixed apocrine carcinoma	1	4	100	0	1 limb	1 Mongrel	16
Apocrine ductal carcinoma	2	9	0	100	1 of each perianal ant tail	1 of each Cocker spaniel and German shepherd dog	8
Total	**23**	**100**					
Anal sac gland carcinoma	5		40	60	5 peranal	2 Mongrel and 1 of each Golden retriever, Cocker spaniel and Westhighland white terrier	11

4.1.8.10. Melanocytic Tumors

43 melanocytic tumors were found in our collection. Melanoacanthoma and melanocytic hyperplasias were not found.

In some heavily pigmented cases, melanin bleach was used to facilitate the evaluation of the malignancy. In addition, two suspected cases of amelanotic malignant melanomas were confirmed immunohistologically, which expressed vimentin, Melan A and S100, and were negatively for cytokeratin, CD3 and CD79α.

4.1.8.10.1. Melanocytoma

20 tumors were found in 12 males (60%) and 8 females (40%), and one dog was without data. 19 tumors were located as follows: 8 at the head, 5 at limbs (two at thigh, one each at arm, paw, shoulder), 5 at back and two in abdomen and for one tumor there were no data of location. The dogs were 5 Mongrels and two of each Golden retriever and Roughhaired dachshund, and one Bernese mountain dog, Boxer, Dachshund, Poodle, Rottweiler, German shepherd dog, Canadian shepherd dog, Giant schnauzer, Softcoated wheaten terrier and Yorkshire terrier, and one dog was without breed data. Age varied between 4 and 14-years-old with a mean of 8 years, and for one dog there were no age data.

4.1.8.10.2. Malignant melanoma

22 tumors were found in 12 females (55 %) and 10 males (45 %). The tumors were located as follows: 9 at head, 7 at limbs (all at paw), two perianal, and one at abdomen, back and neck and one tumor was without data of location. The dogs were 7 Mongrels, two of each Poodle, German shepherd dog and Cocker spaniel, and one of each Bayrischer gebirgsschweisshund, Bordeaux dog, Lahaso apso, Golden retriever, Rottweiler, Giant schnauzer, Setter, Scotch terrier and Wolfshound. The ages varied between 3 and 14 years with a mean of 10 years.

4.1.8.11. Tumors of Fibrous Tissue

Collagenous hamartoma was also listed above with the other hamartomas (see 4.1.8.4). Nodular dermatofibrosis of the German shepherd dog, nodular fasciitis and malignant fibrous histiocytoma were not found in this collection. The other types are represented in table 21.

One case of an atypical tumor located in the axillary region of a male, 12-year-old, Mongrel dog. This case showed a different size of empty areas in myxofibroma-like tumor. By use of immunohistological techniques, the wall of the empty areas expressed Factor VIII, and the

tumor cells that were found in the myxofibroma-like tumor expressed factor VIII and vimentin. This case was sorted as a myxoma in the table 21.

Tab. 21: Fibrous tissue tumors (n=63)

Tumor	*n*	*%*	♂ *%*	♀ *%*	*Location*	*Breed*	*Age in years (mean)*
Fibroma	11	17	45	55	7 limb, 2 head, 1 neck and 1 all body	5 Mongrel and 1 of each Dalmatin, Labrador, Golden Retriever, Bull Terrier and Yorkshire Terrier*	10
Collagenous hamartoma	13	21	38	62	***	***	***
Myxoma	2	3	100	0	1 head	1 Bobtail	8
Fibrosarcoma	32	51	66	34	16 limb, 5 head, 4 chest, 2 perianal, 1 of each back and neck**	8 Mongrel, 6 German shepherd dog, 2 Boxer, and 1 of each Afgahne, Altdeutscher huetehund, Bernese mountain dog, Long-hair dachshund, Rough-haired dachshund, German wirehaired pointer, Dobermann, Muensterlaender, Pinscher, Golden Retriever, Schnauzer, Giant schnauzer, Airedale terrier, Cairn terrier, Fox terrier and Kerry blue terrier	9
Myxosarcoma	5	8	80	20	2 of each abdomen and head, and 1 chest	1 of each Boxer, Roughhaired dachshund, Mongrel, American shepherd, Canadian shepherd and Bedlington terrier	10

* One case without data of breed.
** One case without data of location.
*** Was mentioned above (see 4.1.8.4)

4.1.8.12. Tumors of adipose tissue

Neither angiolipoma nor any of the liposarcomas were found in this collection. A total of 46 lipomas were found in 29 females (63 %) and 17 males (37 %), two of which were diagnosed as infiltrative lipomas. The tumors were located as follows: 13 at the chest, 10 at the limbs, 8 at the abdomen, three each at the back, the mammary gland region, the neck, two at the head and one each at the perianal and the tail and one tumor was without data of location. The dogs were 17 Mongrels, and three Roughhaired dachshunds, Westhighland white terriers, 2 Bernese mountain dogs, and one Akita, Saint bernard, Bobtail, Longhaired dachshund, Dobermann, Huetehund, Husky, Labrador, Malamute, Maltese dog, Mastiff, Munsterlaender (breed not further specified), Small munsterlaender, Retriever, Rottweiler, German shepherd dog, Miniature schnauzer, Setter, Cocker spaniel, Terrier (breed not further specified) and Fox terrier. The ages were from 4 to 16-years-old with a mean of 9 years.

4.1.8.13. Tumors of muscle

Of this group, only one leiomyosarcoma was found in our collection, and it was found at the neck of an 11-years-old male Cocker spaniel. The tumor was examined immunohistologically, and expressed smooth muscle actin, vimentin and few cells expressed S100. The tumor cells were expressed negatively with cytokeratin, CD3, CD79α, IgG, lysozyme, Melan A and desmin.

4.1.8.14. Tumors of vascular tissue

Vascular tissue tumors are presented in table 22. Scrotal vascular hamartoma, Kaposi-like vascular tumor and lymphangiosarcoma were not found in our collection.

Tab. 22: Vascular tissue tumors (n=26)

Tumor	*n*	*%*	♂ *%*	♀ *%*	*Location*	*Breed*	*Age in years (mean)*
Hemangioma	19	73	58	42	5 limb, 3 neck, 2 of each abdomen, back and chest, and 1 of each head, mammary gland region and tail*	6 German shepherd dog 3 of each Roughhaired dachshund and Mongrel, and 1 of each Bernese mountain dog, Boxer, Dachshund, German shorthaired pointer, Hovawart, Belgischer shepherd and Shi-tzu	9
Hemangiosarcoma	7	27	86	14	4 neck, 1 of each chest, limb and head	2 of each German shepherd dog, Westhighland white terrier and Mongrel, and 1 Basset	11

***** Two cases without data of location.

4.1.8.15. Tumors of Peripheral Nerves

Two malignant peripheral nerve sheath tumors (MPNST) of the skin and subcutis were found, the other types were not found in this collection. The tumors were found in two males, one 10-year-old German shepherd dog and one 9-year-old beagle. One tumor was located at limb and one at the neck. Both tumors were examined immunohistologically and the results are reported in table 23. In the case of the beagle, the nerve remnant was found and it reacted positively with S100 and neurofilament. In the case of the German shepherd dog, the tumor was histologically identical with that described in the literature, i.e., the arrangement of the cells in small interwoven bundles (Hendrick et al., 1998, Goldschmidt and Hendrick, 2002) and the occurrence of spindle-shaped cells that exhibit nuclear palisading (Scott et al., 2001).

Tab. 23: Immunohistological examination of MPNST

Tumor/Immunohis.	Vimentin	S100	Neurofilament	Desmin	Smooth muscle actin	Actin	GFAP	NSE
MPNST, Beagle	++++	-*	-*	-	+	++	++	++++
MPNST, German shepherd dog	++++	++	-	-	+	++	-	+++

*Only the nerve remnant reacted positively (+++)

4.1.8.16. Tumors of the synovium and mesothelium

Mesothelium tumors were not found in this collection, and only two synovial cell sarcomas were found at the limbs (knee joint and toe) of two males, a 7-year-old Bernese mountain dog and an 8-year-old Mongrel.

4.1.8.17. Mast cell tumors

56 cases are summarized in table 24. In all cases of grade III, the diagnosis of mast cell tumor was confirmed by using Toluidin stain, which demonstrated the metachromasy of the granules in the neoplastic mast cells.

Tab. 24: Mast cell tumors (n=56)

Tumor	*n*	*%*	♂ *%*	♀ *%*	*Location*	*Breed*	*Age in years (mean)*
Canine, grade I	25	45	48	52	10 limb, 4 chest, 3 head, 2 in each neck and abdomen, and 1 in each back, mammary gland region and perianal*	6 Mongrel, 4 Golden retriever, 3 Boxer, 2 of each Bernese mountain dog, Labrador and Staffordshire terrier, and 1 of each Cocker spaniel, Pitbull, Rottweiler, Siberian husky and Westhighland white terrier*	7
Canine, grade II	22	39	62	38**	13 limb, 4 abdomen, 2 head and 1 in each back, chest and neck	5 Boxer, 4 Mongrel, 3 Staffordshire terrier, 2 Bernese mountain dog and 1 of each American staffordshire terrier, Bull terrier, Golden retriever, Longhair dachshund, Roughhaired dachshund and Springer spaniel**	8**
Canine, grade III	9	16	67	33	4 limb, 3 head and 1 perianal***	2 Cocker spaniel and 1 of each Bernese mountain dog, Boxer, German shepherd dog, Dachshund, Eurasier, Pitbull and Golden retriever	10

* One case without data of location, one without data of breed.
** One case without data of sex, one without data of age and one without data of breed.
*** One case without data of location.

4.1.8.18. Histiocytic tumors

These tumors were represented also in the table 25, and note that for one canine cutaneous histiocytoma there were no data of sex, for two no data of location, for 5 no data of breed and for three no data of age. Xanthoma and systemic histiocytosis were not found in our collection.

Many suspected cases were confirmed immunohistologically, which expressed vimentin, lysozyme, MAC387 and MHC II. In many cases some other immunohistological stains, as S100, factor VIII-related antigen, IgG, cytokeratin, desmin, Melan A, were applied and were negative.

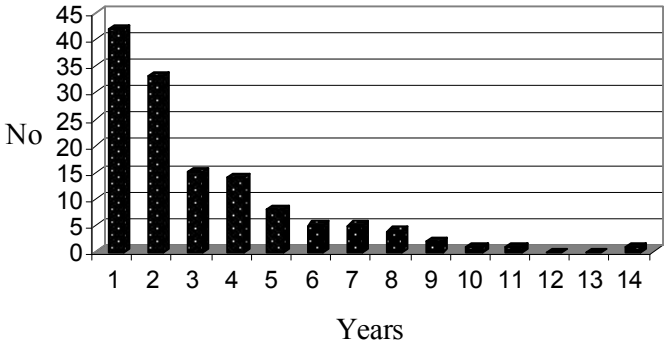
Tab. 25: Histiocytic tumors (n=141)

Tumor	*n*	*%*	♂ *%*	♀ *%*	*Location*	*Breed*	*Age in years (mean)*
Canine cutaneous histiocytoma	134	95	67	33	54 head, 46 limb, 11 chest, 6 in each abdomen and neck, 4 back, 2 perianal and 1 in each mammary gland region and tail	*	3
Cutaneous histiocytosis	3	2	100	0	2 limb and 1 neck	1 in each Newfoundland, Cocker spaniel and Dachshund	10
Malignant histiocytosis	4	3	25	75	3 limb and 1 chest	4 Bernese mountain dog	7
Total	**141**	**100**					

* 30 Mongrels, 8 of each Dobermann and Boxer, 7 Golden retrievers, 5 of each Westhighland white terrier and Rottweiler, 4 of each Jack russel terrier, German shepherd dog and Cocker spaniel, three of each Roughhaired dachshund, Labrador retriever, Bernese mountain dog and beagle, two of each Tibetan terrier, Setter, Pit bull terrier, Newfoundland, Bulldog and Border collie, and one of each Yorkshire terrier, Wolfsspitz, Terrier (breed not further specified), Staffordshire terrier, Stafford bullterrier, Scotch terrier, Schwarzwaldbracke, Giant schnauzer, Poodle, Pon, Pinscher, Pitbull, Kuvasz, Hunting terrier, Irish setter, Husky, Hannoverscher Schweisshund, Gordon setter, French bulldog, Dogge, German wirehaired pointer, German dogge, Dalmatian, Collie, Bordeaux dog, Bobtail, Bearded collie, Australian shepherd dog, American staffordshire terrier and American bulldog.

The diagram 8 shows the age distribution for canine cutaneous histiocytoma.

Diag. 8: Age distribution of canine cutaneous histiocytoma (n=134)



4.1.8.19. Calcinosis circumscripta

13 lesions were found in 7 females (58 %) and 5 males (42 %), and for one dog the sex was not stated. These lesions were located as follows: 9 at limbs (5 paws, two in elbows and one in each tarsal joint and shoulder), one at back, chest and neck and one lesion had no data of location. 4 dogs were German shepherd dogs, three of each Mongrel and Rottweiler, and one each of Appenzeller, Boxer and Irish wolfhound. They were between one and 6-years-old, with a mean of three years, and for one dog no age data were available.

4.1.8.20. Canine hemangiopericytoma

19 cases were found in 10 females (53 %) and 9 males (47 %), and they were located as follows: 14 at limbs, two in each chest and head and one in abdomen. The dogs were 6 Mongrels, two German shepherd dogs, and one of each Boxer, German wirehaired pointer, Dobermann, Munsterlaender (breed not further specified), Large munsterlaender, Small munsterlaender, Golden retriever, Setter, Hunting terrier and Wachtel dog, and one dog for which there were no data of breed. The dogs were between 3 and 12-years-old, with a mean of 9 years.

4.2. Tumors in cat

In this part, we present 197 skin tumors and tumor-like lesions of 194 cats as follows:

4.2.1. Sex distribution

Out of 194 cats, 4 were without data of sex, the remainder was distributed as in table 26.

Tab. 26: Sex distribution in cats (n=190)

Sex	*Castrated*	*Non castrated*	*Total*	*%*
♂	53	52	105	55.3
♀	28	57	85	44.7

4.2.2. Anatomical location

Out of 197 feline skin tumors and tumor-like lesions, only two were without data concerning location, the remainder was distributed as in table 27.

Tab. 27: Location distribution (n=195)

Location	*n*	*%*
Limb	49	25
Head	48	25
Back	35	18
Chest	28	14.
Neck	16	8
Abdominal	12	6.
Perianal	5	3
Mammary Area	1	1
Tail	1	1
All Body	0	0

4.2.3. Breed disposition

For 49 out of 194 cats no data of breed were available, the remainder was distributed as in table 28.

Tab. 28: Breed disposition (n=145)

Cat breed	*n*	*%*
ESH cat	122	84
Persian	11	8
Maine-coon cat	6	4
Karthaeuser „British blue“	3	2
Angora cat	1	1
Birma	1	1
Siam	1	1

4.2.4. Age of distribution

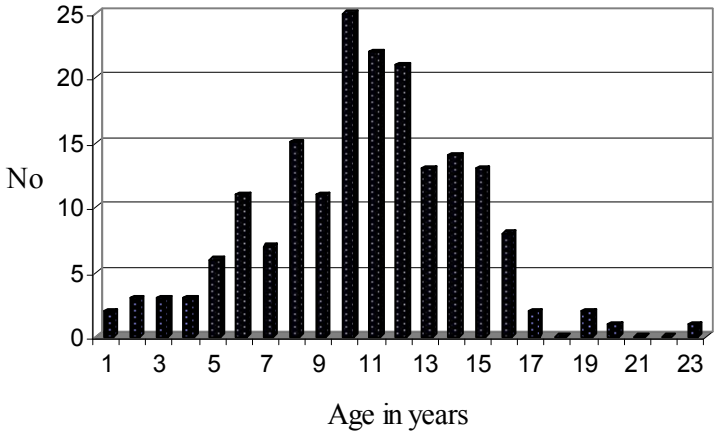
11 out of 194 cats were of unknown age; the remainder was distributed as in table 29 and diagram 9.

Tab. 29: Age distribution in years (n=183)

Age	1	2	3	4	5	6	7	8	9	10	11	12
n	2	3	3	3	6	11	7	15	11	25	22	21
%	1.0	1.5	1.5	1.5	3.5	6.0	4.0	8.0	6.0	14.0	12.0	11.5

Age	13	14	15	16	17	18	19	20	21	22	23
n	13	14	13	8	2	0	2	1	0	0	1
%	7.0	8.0	7.0	4.5	1.0	0.0	1.0	0.5	0.0	0.0	0.5

Diag. 9: Age distribution in cats (n=183)

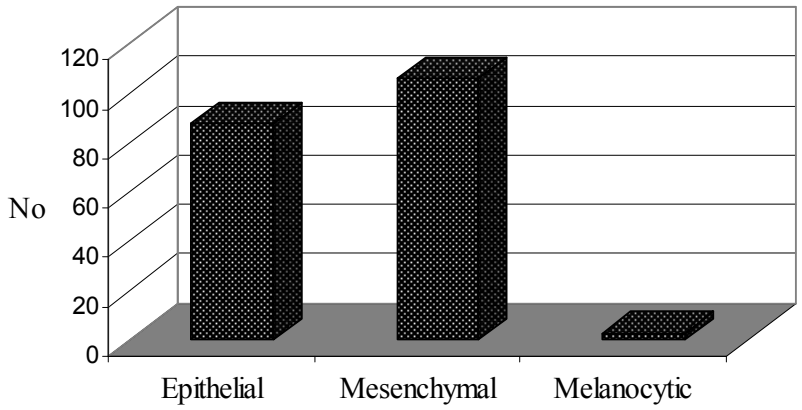


The diagram shows a gradual increase over the first 10 years with a peak at the age of 10, then a gradual drop over the next 7 years of age, and scattered cases are found in the age group between 19 and 23 years.

4.2.5. Origin of tumors and tumor-like lesions

Epithelial, mesenchymal and melanocytic origins were the three main groups according to the WHO classification; the tumor-like lesions were distributed under the three groups and the results are shown in diagram 10.

Diag. 10: Origin of tumors and tumor-like lesions (n=197)



The diagram shows the origin of three tumor groups, 106 tumors were of mesenchymal origin (54 %), 88 tumors of epithelial origin (45 %), and 3 tumors of melanocytic origin (1 %).

4.2.6. Prevalence of individual groups of skin tumors

197 skin tumors and tumor-like lesions are divided in groups according to the new WHO classification, as in table 30.

The table shows in descending order the numbers and percentages of the tumors and exposes at the top the more common group, namely tumors of fibrous tissue. However, for 9 tumor groups no instances were found, namely histiocytic, miscellaneous and unclassified tumors, tumors of smooth muscle, tumors metastatic to the skin, tumors of striated muscle, tumors of peripheral nerves, tumors of synovium and tumors of mesothelium.

Tab. 30: Prevalence of individual groups of skin tumors (n=197)

Tumor	*n*	*%*
Tumors of fibrous tissue	79	40.0
Tumors with adnexal differentiation	51	26.0
Tumors of the epidermis	18	9.0
Epithelial tumors without sqamous or adnexal differentiation	11	5.5
Tumors of vascular tissue	11	5.5
Tumors of adipose tissue	10	5.0
Mast cell tumors	6	3.0
Cysts	3	1.5
Tumor-like lesions	3	1.5
Melanocytic tumors	3	1.5
Hamartomas	2	1.0

4.2.7. Prevalence of individual types of skin tumors

110 types of the skin tumors and tumor-like lesions in all animal species in accordance with the new WHO classification were reported; 31 types were found in the cats of our collection and 19 of these are listed in table 31, in descending order of number and percentages of the tumors. The other 12 types were represented by only one case (0.5 %) each; they were multicentric squamous cell carcinoma in situ, trichoepithelioma, sebaceous adenoma, sebaceous carcinoma, complex and mixed apocrine adenoma, complex and mixed apocrine carcinoma, ceruminous adenoma, anal sac gland carcinoma, fibroepithelial "polyp", melanocytoma, myxoma and Feline ventral abdominal angiosarcoma.

79 types were not found in this collection, and some of them were species-specific or rare or not reported in cats. Tumors that were not found in cats in our collection were papilloma, inverted papilloma, basosquamous carcinoma, tricholemmoma, malignant trichoepithelioma, pilomatricoma, malignant pilomatricoma, subungual keratoacanthoma, sebaceous epithelioma, meibomian adenoma, meibomian ductal adenoma, meibomian epithelioma, meibomian carcinoma, apocrine ductal carcinoma, complex and mixed ceruminous adenoma, complex and mixed ceruminous carcinoma, anal sac gland adenoma, eccrine adenoma, eccrine carcinoma, fibroma, melanoacanthoma, malignant fibrous histiocytoma, angiolipoma, liposarcoma, leiomyoma, leiomyosarcoma, rhabdomyoma, rhabdomyosarcoma, lymphangioma, Kaposi-like vascular tumor, lymphangiosarcoma, granular cell tumor, benign and malignant peripheral nerve sheath tumor of skin and subcutis, synovial cell sarcoma, mesothelioma, malignant histiocytosis, and malignant mesenchymoma. Tumor-like lesions that were not found in cats in our collection were dilated pore, isthmus cyst, panfollicular cyst, dermoid cyst, sebaceous duct cyst, apocrine cyst and cystomatosis, ciliated cyst, subungual epithelial inclusion cyst, epidermal hamartoma, sebaceous hamartoma, apocrine hamartoma, fibroadnexal hamartoma, squamous papilloma, pressure point comedones, cutaneous horn, warty dyskeratoma, fibropruritic nodule, melanocytic hyperplasia, collagenous hamartoma, nodular fasciitis, scrotal vascular hamartoma, traumatic neuroma, xanthoma, calcinosis circumscripta

Tab. 31: Prevalence of 19 types of skin and soft tissue tumors and tumor-like lesions in cats (n=185)

Tumor	*n*	*%*
Fibrosarcoma	74	37.5
Squamous cell carcinoma	17	8.5
Apocrine adenoma	14	7.0
Basal cell tumor	11	5.5
Lipoma	10	5.0
Trichoblastoma	9	4.5
Ceruminous gland carcinoma	7	3.5
Hemangiosarcoma	7	3.5
Apocrine carcinoma	6	3.0
Feline mast cell tumor	6	3.0
Apocrine ductal adenoma	4	2.0
Myxosarcoma	4	2.0
Infundibular cyst	3	1.5
Hemangioma	3	1.5
Subungual squamous cell carcinoma	2	1.0
Sebaceous ductal adenoma	2	1.0
Follicular hamartoma	2	1.0
Sebaceous hyperplasia	2	1.0
Malignant melanoma	2	1.0

Some other tumors were found in the skin and subcutaneous tissue, but were not considered in our collection because they had not been classified under skin and soft tissue tumors in the new WHO classification. They were 4 extramedullary plasmocytomas, 4 lymphosarcomas, three which could not be classified, and one meibomian gland hyperplasia.

4.2.8. Entities of skin tumors and tumor-like lesions

4.2.8.1. Basal cell tumors

11 basal cell tumors were found in 7 males (64 %) and 4 females (36 %), and they were located as follows: three at the limbs, two each at the back, chest and neck, and one each at head and perianal region. The cats were 5 ESH cats, and one of each Birma, Maine-coon and Persian cats, and for three cats there were no data of breed. The cats were aged between 7 and 23 years with a mean age of 13 years. 8 out of 11 basal cell tumors (73 %) showed cystic degeneration (cystic basal cell tumor).

4.2.8.2. Tumors of the Epidermis

17 squamous cell carcinomas were found under this group, and they were found in 9 female (56 %), 7 male (44 %), and for one cat the sex was not stated. The tumors located as follows: 12 at the head (7 auricle, 2 eyelid, 2 mandible region and one cheek), three at the limbs, and one each at the mammary gland and perianal regions. The cats were 13 ESH cats, and for 4 cats there were no data of breed. For two cats there were no age data, the others were between one and 16-years-old, with a mean of 9 years.

One multicentric squamous cell carcinoma in situ was found in the paw of a female 15-year-old ESH cat.

4.2.8.3. Follicular tumors

Two follicular tumor types were found in the cats of this collection, namely trichoblastoma and trichoepithelioma.

4.2.8.3.1. Trichoblastoma

There were 9 cases, and they were found in 8 males (89 %) and one female (11 %). 6 tumors were located at limbs (4 shoulder and 2 paw), and one each at chest, head and tail. One cat was without data regarding breed, the other were 6 ESH cats, two Maine-coon cats. Two cats were 13-years-old and one cat was 6, 7, 9, 11, 12, 15 years, respectively, and for one cat there were no age data. The mean age was 11 years.

Tab. 32: Trichoblastom variants (n=9)

Tumor variant	*n*	*%*
Ribbon	1	11
Spendle	2	22
Granular	0	0
Trabecular	6	67
Mixed	0	0

4.2.8.3.1.1. Cystic degeneration of trichoblastomas

Two cases out of 9 feline trichoblastomas in our collection showed this manifestation, and these were one case of ribbon and one of trabecular variant in cats. In the case of ribbon variant, cystic degeneration was found at the center of solid lobules, with an accumulation of light brown necrotic debris. In some instances, the presence of a few brown pigments and calcifications at the center of the cysts was detected, which was surrounded by a zone of viable, less basophilic tumor cells. The trabecular case exhibited the same changes, but at the

same time showed more mucinous degenerations of tumor cells and plenty of mucinous substances surrounded the tumor pattern.

4.2.8.3.2. Trichoepithelioma

The trichoepithelioma reported in our collection was a single case in the shoulder of a 9-year-old male ESH cat.

4.2.8.4. Nailbed tumors

Only two subungual squamous cell carcinomas were found in this collection, and they were located in the paws of a 10-year-old female ESH cat and a 7-year-old female cat without breed data.

4.2.8.5. Sebaceous and modified sebaceous gland tumors

Three tumor types were found in this collection and represented as in table 33.

Tab. 33: Sebaceous and modified sebaceous gland tumors (n=4)

Tumor	*n*	*%*	*♂ %*	*♀ %*	*Location*	*Breed*	*Age in years (mean)*
Sebaceous adenoma	1	25	0	100	1 head	1 Angora cat	10
Sebaceous ductal adenoma	2	50	50	50	1 in each chest and back	2 ESH cats	14*
Sebaceous carcinoma	1	25	100	0	1 limb	1 Persian	16

* 1 case without data of age.

4.2.8.6. Apocrine, modified apocrine and eccrine gland tumors

Eccrin tumors, apocrine ductal carcinoma, complex and mixed ceruminous adenoma, complex and mixed ceruminous carcinoma and anal sac gland adenoma were not found in this collection. Other apocrine and modified apocrine gland tumors were represented in table 34.

Tab. 34: Apocrine, modified apocrine and eccrine gland tumors (n=35)

Tumor	*n*	*%*	♂ *%*	♀ *%*	*Location*	*Breed*	*Age in years (mean)*
Apocrine adenoma	14	40	46	62*	6 head, 3 in each back and neck, and 1 in each chest and limb	10 ESH cats and 1 Perser*	11*
Complex and mixed apocrine adenoma	1	3	100	0	1 head	1 ESH cat	14
Apocrine ductal adenoma	4	11	25	75	3 head, 1 neck	3 ESH cats**	13
Apocrine carcinoma	6	17	50	50	2 head, 1 in each back, limb, neck and perianal	5 ESH cats**	14
Complex and mixed apocrine carcinoma	1	3	100	0	1 chest	Unknown	12
Ceruminous adenoma	1	3	0	100	1 head	1 ESH cats	12
Ceruminous gland carcinoma	7	20	57	43	7 head (auricle)	6 ESH cats**	11
Anal sac gland carcinoma	1	3	100	0	1 perianal	1 ESH cat	15

* One case without data of sex, two cases without data of age and three cases without data of breed.
** One case without data of breed.

4.2.8.7. Cysts

Infundibular cyst was the only cyst type that was found in cats in our collection. Three cases of infundibular cyst were found in two females and one male. They were located one each at chest, back and neck in three ESH cats that were 2, 10 and 14-years-old, respectively.

4.2.8.8. Hamartomas

Only two follicular hamartomas were found in the cats in our collection. They were found in 11 and 12-year-old female Mongrel cats. The lesions were located at the back and thigh.

4.2.8.9. Tumor-like lesions

Two cases of sebaceous hyperplasia were found in two female ESH cats. One cat was 12-years-old, and the age of the other cat was unknown. The lesions were located at head and chest.

Other tumor-like lesions were not found in this collection.

4.2.8.10. Melanocytic tumors

Melanoacanthoma and melanocytic hyperplasia were not found in the cats in our collection. Melanocytomas and malignant melanoma were represented as in table 35.

Tab. 35: Melanocytic tumors (n=3)

Tumor	*n*	*%*	♂ *%*	♀ *%*	*Location*	*Breed*	*Age in years (mean)*
Melanocytoma	1	33	100	0	1 head	1 ESH cat	12
Malignant melanoma	2	67	100	0	2 head	1 ESH cat*	11

* One case without data of breed.

4.2.8.11. Tumors of fibrous tissue

Myxoma, fibrosarcoma and myxosarcoma were found in the cats in our collection, and were represented as in table 36. Other tumor types were not found in this collection.

Tab. 36: Tumors of fibrous tissue (n=79)

Tumor	*n*	*%*	♂ *%*	♀ *%*	*Location*	*Breed*	*Age in years (mean)*
Myxoma	1	1	0	100	1 limb	1 ESH cat	13
Fibrosarcoma	74	94	59	41	22 back, 15 in each limb (7 shoulder, 5 paw and 3 thigh) and chest, 10 abdomen, 6 neck and 5 head*	43 ESH cats, 5 Persians, and 1 in each Karthaeuser, Maine-coon cat and Siam*	10*
Myxosarcoma	4	5	50	50**	3 limb (2 paw, 1 shoulder) and 1 perianal	2 ESH cat**	11**

* One case without data of location, 23 cases without data of breed and two cases without data of age. ** Two cases without data of sex, two cases without data of breed and one case without data of age.

4.2.8.12. Tumors of adipose tissue

10 lipomas were found in 6 males (60%) and 4 females (40%), and located as follows: three each at limbs and back, two in abdomen and one each at head and neck. The cats were 9 ESH cats and one cat was without data regarding breed. Cats were between 6 and 14-years-old, with a mean of 9 years. Other tumor types of adipose tissue were not found in our collection.

4.2.8.13. Tumors of Vascular Tissue

Hemangioma, hemangiosarcoma and lymphangiosarcoma were found in the cats in this collection and are represented in table 37. Other tumor types were not found in this collection. One suspected case of hemangiosarcoma was confirmed immunohistologically, which expressed factor VIII-related antigen, and negative for cytokeratin

Tab. 37: Tumors of Vascular Tissue (n=11)

Tumor	*n*	*%*	♂ *%*	♀ *%*	*Location*	*Breed*	*Age in years (mean)*
Hemangioma	3	27	0	100	2 limb and 1 head	Unknown	8
Hemangiosarcoma	7	64	71	29	2 at each chest and limb, 1 at each abdomen, head and neck	4 ESH cats	11**
Feline ventral abdominal angiosarcoma	1	9	100	0	1 chest	1 ESH cat	15

* Three cases without data of breed.
** One case without age data.

4.2.8.14. Feline mast cell tumors

6 mast cell tumors were found in three females (50%) and three males (50%), and two tumors were located each at limb, head and back. The cats were two each Persian and ESH cats and one Maine-coon cat, and one cat was without data of breed. They were between two and 15-years-old, with a mean value of 9 years. One tumor showed a high mitotic rate (3 to 5 in high power field (40X)), the others showed very few mitotic figures. The diagnosis of feline mast cell tumor was in all cases confirmed by using Toluidin stain.

5. DISCUSSION

Because lesions and masses involving the skin are easily seen by the owner and brought to the attention of the veterinarian, these lesions will frequently be removed and submitted for histopathologic evaluation. Skin tumors including epithelial, melanocytic and mesenchymal neoplasms and non-neoplastic lesions are very common, particulary in the dog and cat, and they are the most commonly diagnosed tumors in domestic animals, at least at our institute.

In 1974, the World Health Organization (WHO) published a text on the international histological classification of tumors of domestic animals, which followed, as far as possible, the WHO histological classifications of tumors in man. This classification contained also tumors of the skin and was reported by Weiss and Frese (1974) and Weiss (1974).

A new or second edition of the international histological classification of skin, melanocytic and soft tissues tumors of domestic animals was published by Goldschmidt et al. (1998) and Hendrick et al. (1998) with new entities and some new nomenclatures. For the time between 1998 and today, we have not found any statistical study that exposes all these tumors according to the new WHO classification. Therefore, the purpose of this study is to apply the new WHO classification to the epidemiology of skin tumor entities in dogs and cats.

In this study we will expose the general and the individual prevalence of skin tumors and tumor-like lesion according to the new WHO and discuss and compare the results with other older studies that were performed by other authors. In addition, we will interpret and classify the new terms in the new WHO classification. Afterwards we will expose the classification problems of some skin lesions according to the new WHO classification and report some skin tumors that are not found in the new WHO classification

5.1. General prevalence of skin tumors and tumor-like lesion

The present study was carried out on 816 canine and 194 feline skin tumors and tumor-like lesions from 768 dogs and 194 cats. The prevalence of skin tumors and tumor-like lesions in dogs and cats was different when compared with previous studies carried out by many authors (Frese, 1960, Eskens, 1983, Goldschmidt and Shofer, 1992, Bomhard, 2001). This may be explained by the fact that we used the new WHO classification in our study (Goldschmidt et al., 1998, Hendrick et al., 1998) whereas in the recent study by Bomhard (2001) the nomenclature followed the first WHO classification, although deviating in some points, in spite of the fact that this work was done in 2001.

Because we have not found a specific statistical definition of the terms common, uncommon and rare, we divide skin tumors according to the following categorization: Tumors that are not found in our collection seem to be rare. Tumors found in less than 1 % (less than 8 cases in dogs and two in cats in our study) seem to be uncommon and those found in 1 % or more seem to be common.

5.1.1. Prevalence of skin tumors according to the new WHO classification

5.1.1.1. In dog

The first 10 common skin tumors and tumor-like lesions were canine cutaneous histiocytoma (16.4 %), mast cell tumor (6.9 %), lipoma (5.6 %), hepatoid gland adenoma (5.4 %), infundibular cyst (4.5 %), fibrosarcoma (3.9 %), sebaceous hyperplasia (2.8 %), malignant melanoma (2.7 %), trichoepithelioma (2.7 %) and melanocytomas (2.6 %). Less common tumors, which had a prevalence between 2.6 % and 0.9 %, were meibomian adenoma, canine hemangiopericytoma, hemangioma, infundibular keratinizing acanthoma, apocrine cyst, sebaceous adenoma, subungual squamous cell carcinoma, trichoblastoma, pilomatricoma, calcinosis circumscripta, collagenous hamartoma, fibroma, fibropruritic nodule, panfollicular cyst, sebaceous duct cyst, follicular hamartoma, basosquamous carcinoma, fibroepithelial "polyp", papilloma, squamous papilloma and fibroadnexal hamartoma consecutively. Uncommon tumors, with a prevalence of less than 1 %, were apocrine ductal adenoma, hemangiosarcoma, squamous cell carcinoma, anal sac gland carcinoma, apocrine adenoma, apocrine carcinoma, basal cell tumor, hepatoid gland epithelioma, myxosarcoma, sebaceous epithelioma, dermoid cyst, isthmus cyst, malignant histiocytosis, sebaceous hamartoma, complex and mixed apocrine adenoma, cutaneous histiocytosis, apocrine ductal carcinoma, malignant peripheral nerve sheath tumor of the skin and subcutis, meibomian carcinoma, meibomian epithelioma, sebaceous carcinoma, subungual epithelial inclusion cyst, subungual keratoacanthoma and synovial cell sarcoma. 9 types were represented only by one case each (0.1 %). Single cases that found in our collection seem to be uncommon. These types were apocrine hamartoma, complex and mixed apocrine carcinoma, hepatoid gland carcinoma, leiomyosarcoma, lymphangioma, malignant trichoepithelioma, multicentric squamous cell carcinoma in situ, myxoma, and pressure point comedones. The other 38 types were not found in our collection and seem to be rare, and for some of these only a few cases had been reported in the literature (Goldschmidt et al., 1998, Hendrick et al., 1998, Goldschmidt and Hendrick, 2002). The tumors that were not found in our collection were anal sac gland adenoma, angiolipoma, basal cell carcinoma, benign peripheral nerve sheath tumor of skin

and subcutis, ceruminous adenoma, ceruminous gland carcinoma, complex and mixed ceruminous carcinoma, complex and mixed ceruminous adenoma, eccrine adenoma, eccrine carcinoma, granular cell tumor, inverted papilloma, Kaposi-like vascular tumor, leiomyoma, liposarcoma, lymphangiosarcoma, malignant fibrous histiocytoma, malignant mesenchymoma, malignant pilomatricoma, meibomian ductal adenoma, melanoacanthoma, mesothelioma, rhabdomyoma, rhabdomyosarcoma, sebaceous ductal adenoma, systemic histiocytosis and tricholemmoma. The tumor-like lesions that were not found in the dogs of our collection were traumatic neuroma, scrotal vascular hamartoma, nodular dermatofibrosis of the German shepherd dog, nodular fasciitis, melanocytic hyperplasia, epidermal hamartoma, cutaneous horn, dilated pore, ciliated cyst, warty dyskeratoma and xanthoma.

We can expose some tumors with marked changes in prevalence due to the new WHO classification compared with the results from Frese (1960), Eskens (1983), Goldschmidt and Shofer (1992) and Bomhard (2001) as following:

5.1.1.1.1. Squamos cell carcinoma

The prevalence of the squamous cell carcinoma in many previous studies, varied between 1.7 % and 7.25 %, and was 7.25 % according to Frese (1960), 2.31 % according to Eskens (1983), 1.7 % according to Goldschmidt and Shofer (1992) and 2.97 % according to Bomhard (2001), and it constitutes 3 % of all skin tumors and tumor-like lesion in our study. However, according to the new WHO classification, it is subdivided into two types, squamous cell carcinoma and subungual squamous cell carcinoma. Squamous cell carcinomas represent 0.9 % of all skin tumors and tumor-like lesions, and seem to be uncommon; however, subungual squamous cell carcinomas are listed under the common skin tumors because they have been observed in 2.1 % of all skin tumors and tumor-like lesions in our study.

5.1.1.1.2. Basal cell tumor

The old term basal cell tumor was mentioned as a common skin tumor and varied between 2 % and 5.9 %, which was 2 % according to Frese (1960), 5.84 % in Eskens (1983), 3.7 % in Goldschmidt and Shofer (1992) and 5.9 % in Bomhard (2001). It was represented in 3.6 % of all cases examined in our study. 55.6 % of those cases were reclassified as trichoblastoma and 27.8 % were reclassified as basosquamous carcinoma according to the new WHO classification. Only 16.7 % were diagnosed as basal cell tumors, which constitute 0.6 % of all

skin tumors and tumor-like lesion in our study. Therefore, the newly classified basal cell tumors seem to be uncommon in dogs.

5.1.1.1.3. Hepatoid gland adenoma

This adenoma has decreased chronologically from the most common skin tumor at about 18 % (Frese, 1960) to 9 % (Eskens, 1983, Goldschmidt and Shofer, 1992) to less than 6 % (Bomhard, 2001) and to 5.4 % in our study. The tumor is testosterone-dependent (Scott et al., 2001). Therefore, an increasing rate of early castration will logically have an effect on the ratio of these tumors. We think that castration of pet animals has increased over time which can explain the decrease of this tumor.

5.1.1.1.4. Sebaceous adenoma

Sebaceous adenoma was applied to a common skin tumor in the literature as well as in our study, which is always placed among the 10 most common skin tumors (Frese, 1960, Eskens, 1983, Goldschmidt and Shofer, 1992, Bomhard, 2001). However, according to the new WHO classification approach applied in our study, more than 22 % of these tumors have been classified as sebaceous epitheliomas. The other 78 % have been classified as sebaceous adenomas, which are less common than in the above literature.

Tab. 38: Sebaceous adenoma and epithelioma

	n	*%*	♂ *%*	♀ *%*
Sebaceous adenoma	17	71	65	35
Sebaceous epithelioma	5	21	100	0

5.1.1.1.5. Follicular tumors

Compared with prevalence studies carried out by many authors (Frese, 1960, Eskens, 1983, Goldschmidt and Shofer, 1992), follicular tumors are far more common in this study. This may be explained by the new WHO classification approach used in this study as in the case of trichoblastoma.

5.1.1.2. In cats

Only 31 types of skin tumors and tumor-like lesions were found in cats in our collection and that may be due to the relative smallness of our collection and the rarity or absence of some tumors in cats. Fibrosarcoma was the most common skin tumor (37.5%) followed by other

common skin tumors, represented by squamous cell carcinoma (8.5%), apocrine adenoma (7.0%), basal cell tumor (5.5 %), lipoma (5.0%), trichoblastoma (4.5%), ceruminous gland carcinoma (3.5 %), hemangiosarcoma (3.5 %), apocrine carcinoma (3.0%) and feline mast cell tumor (3.0%). Less common tumors and tumor-like lesions (between 1 and 2 %) were apocrine ductal adenoma, myxosarcoma, infundibular cyst, hemangioma, subungual squamous cell carcinoma, sebaceous ductal adenoma, follicular hamartoma, sebaceous hyperplasia and malignant melanoma. The other 12 types were represented by only one case (0.5 %) each, and they seem to be uncommon. These tumors were multicentric squamous cell carcinoma in situ, trichoepithelioma, sebaceous adenoma, sebaceous carcinoma, complex and mixed apocrine adenoma, complex and mixed apocrine carcinoma, ceruminous adenoma, anal sac gland carcinoma, fibroepithelial "polyp", melanocytomas, myxoma and Feline ventral abdominal angiosarcoma.

We found that fibrosarcoma was the most common skin tumor in cats in our study as well as in the literature (Stiglmair-Herb, 1987, Joerger, 1988, Goldschmidt and Shofer, 1992, Bomhard, 2001), and squamous cell carcinoma in our study takes the place of basal cell tumor, which is mentioned as the second most common skin tumor in the cat by the above publications. We demonstrate this change by applying the reclassification of 45 % of basal cell tumor as trichoblastoma, which together represent the second most common skin tumor, which agrees with the results of these authors.

4 cases of malignant lymphoma were excluded from the skin tumors in our study in accordance with the new WHO classification, which classifies them as hematopoietic tumors (Valli et al., 2002). However, it was one of the common skin tumors in the cat in the literature (Stiglmair-Herb, 1987, Joerger, 1988, Goldschmidt and Shofer, 1992, Bomhard, 2001), and would be the same in our study if we did not use the new classification.

No tumor-like lesions were mentioned in Joerger's study (1988), but infundibular cyst was also more common in the other studies than in ours (Goldschmidt and Shofer, 1992, Bomhard, 2001), while apocrine adenoma is more common in our study than in others (Stiglmair-Herb, 1987, Joerger, 1988, Goldschmidt and Shofer, 1992, Bomhard, 2001), and note that apocrine ductal adenoma was not mentioned by Stiglmair-Herb (1987), Joerger (1988) and Bomhard (2001) and may have been categorized under apocrine adenoma.

The statistical ratio of squamous cell carcinoma in the cat was not markedly changed by the newly classified subungual squamous cell carcinoma because this newly classified tumor was present in 10.5% of all squamous cell carcinomas.

Another study carried out by Miller et al. (1991) showed different results, with basal cell tumor as the most common skin neoplasm recorded in 26.1 % of the cases. Moreover, mast cell tumor and squamous cell carcinoma were more common than fibrosarcoma. This may be explained by the fact that this study by Miller et al. (1991) was carried out in Columbia, while most of the other studies that were carried by Stiglmair-Herb (1987), Joerger (1988), Goldschmidt and Shofer (1992) and Bomhard (2001), were carried out in Germany and the United States of America. So these differences may be explained by the vaccination behaviour and the prevalence of some infections and predisposing factors existing in these countries such as feline leukemia virus and feline sarcoma virus.

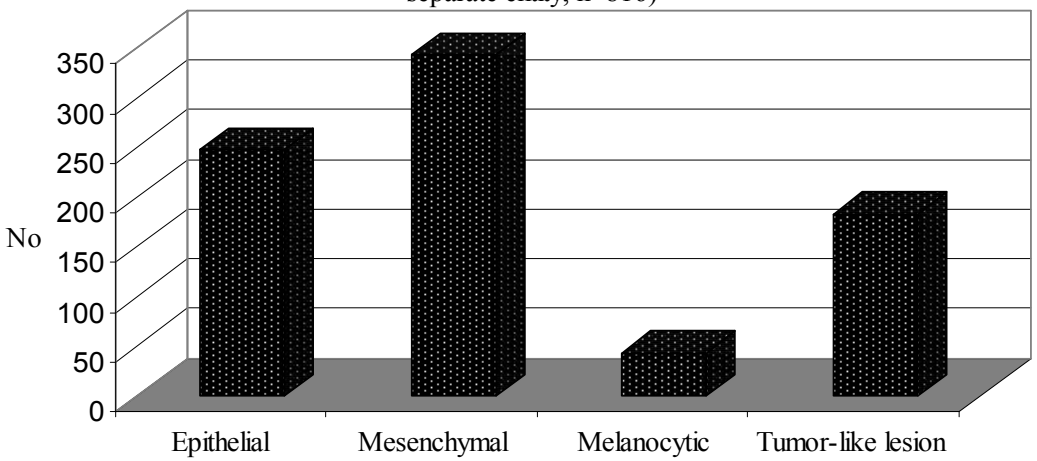
5.1.2. Origin of tumors and tumor-like lesions

5.1.2.1. Dog

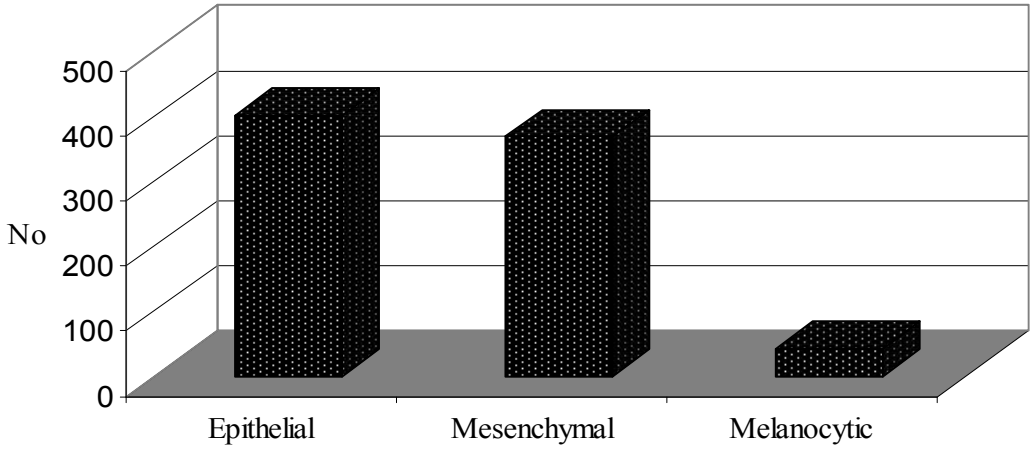
Generally, tumors and tumor-like lesions of the skin were broken down differently by many authors (Frese, 1960, Eskens, 1983, Stiglmair-Herb, 1987, Joerger, 1988, Goldschmidt and Shofer, 1992, Bomhard, 2001). We divided our collection exactly as in the new WHO classification, and therefore we have three groups, including epithelial, melanocytic and mesenchymal tumors. The tumor-like lesions were subsumed under these three groups. If we divide our collection into four groups as is commonly done by some other authors (Eskens, 1983, Goldschmidt and Shofer, 1992), we find significant changes in the dominant kind of the skin tumors in the dog, as in diagram 11 and 12.

183 cases of tumor-like lesions were found in our collection, with 22.4 % of all skin tumors and tumor-like lesions in dogs, which represents the highest reported percentage of tumor-like lesions compared with other statistical studies (Eskens, 1983, Goldschmidt and Shofer, 1992, Bomhard, 2001). Most of these lesions were of epithelial origin. We therefore reporte an increase in the epithelial group after subdivision of the group of tumor-like lesions according to their origins, as in diagram 12. Melanocytic tumors, however, are unchanged, because we did not find any tumor-like lesion of this category in our collection.

Diag. 11: Origin of tumors and tumor-like lesions (tumor-like lesions counted as separate entity, n=816)



Diag. 12: Origin of tumors and tumor-like lesions according to new WHO classification (tumor-like lesion included into the relevant tumor groups, n=816)



We can conclude that the dominant group in dogs is that of the epithelial tumors with 49.3 %, followed by mesenchymal tumors with 45.3 % and melanocytic tumors with 5.3 % of all skin tumors and tumor-like lesion according to the new WHO classification.

5.1.2.1. Cat

In the cat, mesenchymal tumors were always the dominant group and represented 53.8 % of all skin tumors and tumor-like lesions, while 44.7 % of tumors in our study were epithelial in origin, and that was in agreement with the findings in the literature (Stiglmair-Herb, 1987, Willemse, 1991, Goldschmidt and Shofer, 1992). Melanocytic tumors were found in 1.5 % of all skin tumors and tumor-like lesions in cats. All tumor-like lesions in cats were epithelial in

origin; these were only 8 cases (4 %) and they made no great difference regarding the dominance of these groups when they were divided according to the new WHO classification into the mesenchymal, epithelial and melanocytic groups.

5.1.3. Breed disposition

More than 25 % of the dogs in our collection were Mongrels, followed by German shepherd dog (7.2 %), Boxer (4.4 %), Golden retriever (4.0%), Westhighland white terrier (3.6 %), Cocker spaniel (3.5 %), Bernese mountain dog (3.4 %), Rottweiler (2.7 %), Roughhaired dachshund (2.6 %) and Dobermann (2.6 %) and the remaining breeds mentioned in our previous results. Boxer with 16.5 % was the most common breed in the study by Frese (1960), followed by Dachshund 13.2 %, Fox terrier 12.4 % and German shepherd dog 11.8 %. In another study carried out by Walter and Schwegler (1992), cancer was found in 41.9 % of all necropsied Boxers, which showed the highest relative disposition. However, Frese (1960), gave no information on sources (biopsy or necropsy) in his study, and biopsy was the source in our study. On the other hand, the cases of skin tumors and tumor-like lesions in our study as well in the other studies were selected, and that may influence the recognition of breed disposition. Less common breeds are usually more expensive, and the owners of these animals are more often well-to-do, so that animals of these breeds are examined and treated more frequently. This may also apply vice versa to the more common breeds.

The breeds of cats were not available for 49 out of 194 cases in our collection, and we think that all or most of them were Mongrel because with 85 % this breed is the most common in the cat population (Bomhard, 2001) and also with 84 % the most common in our collection. We assume that the senders mostly stated the breeds when they were rare or uncommon breeds. However, to be sure, only 145 cases with known breeds were used in the statistical breed division in our study. The other less common breeds were Persian (7.6 %), Maine-coon cat (4.1 %), Karthaeuser “British blue“ (2.1 %). Angora, Birma, Siam and ESH cats were less than 1 %. It is known that some skin tumors were described only in some breeds or were more common in some breeds, the most common examples being malignant histiocytosis, which was first described in the Bernese mountain dog, but has since been reported in various dog and cat breeds (Goldschmidt and Hendrick, 2002, Court et al., 1993), and nodular dermatofibrosis of the German shepherd dog (Goldschmidt et al., 1998). Another example is mast cell tumor, which is more common in Boxer, Pug and Boston than in other breeds (Goldschmidt and Shofer, 1992, Goldschmidt and Hendrick, 2002).

Regarding nailbed tumors in Standard schnauzer dogs, 11 Standard schnauzer dogs with 12 tumors and tumor-like lesions were found in our collection, of which 7 were nailbed tumors (58 %). These were 5 subungual squamous cell carcinomas and 2 subungual keratoacanthomas which were the only 2 cases in our whole collection. The breed predilection of subungual squamous cell carcinomas in Standard schnauzer dogs and many other breeds was mentioned by Goldschmidt and Hendrick (2002), however, breed predilection of subungual keratoacanthomas in Standard schnauzer dogs has not been reported in veterinary literature (Gross et al., 1992, Goldschmidt et al., 1998, Goldschmidt and Hendrick, 2002).

Cutaneous hemangioma and hemangiosarcomas have a breed predilection for German shepherd dogs (31 %) in our results and shows a higher prevalence in the males (63 %) than in the females of this breed compared to other breeds. We have not found any study that describes and discusses the sex and breed predilection of cutaneous hemangioma and hemangiosarcomas of the skin for the German shepherd dog. However, such predilection is mentioned by other authors for these tumors when occurring in internal organs (Appleby, 1991, Goldschmidt and Hendrick, 2002).

5.1.4. Age distribution

The mean age of animals with skin tumor in our collection was 7.5 years in dogs and 10.6 years in cats. So our results agree with the results of the other authors who state that skin tumors arise above all in old animals (Frese, 1960, Eskens, 1983, Goldschmidt and Shofer, 1992, Bomhard, 2001). At the same time, the results show an exception for dogs with histiocytoma, which have a mean age of 3 years in our study, and this is also reported by many other authors (Eskens, 1983, Goldschmidt and Shofer, 1992, Goldschmidt and Hendrick, 2002). Histiocytoma was always the most common skin tumor in the dog and ranging between 11.5 % and 16.4 % (Eskens, 1983, Goldschmidt and Shofer, 1992, Bomhard, 2001), and it was 16.4 % in our study. Therefore, this tumor has a considerable impact on the general mean age for the occurrence of skin tumors in dogs, and explains the high onset in diagram 13. Some other tumors and tumor-like lesions were considered to be more common in young animals such as papilloma (Goldschmidt and Shofer, 1992, Bomhard, 2001), dermoid cyst and follicular cyst (Bomhard, 2001). In our study papilloma was divided into two forms: papilloma and squamous papilloma, and both lesions seem to occur in young dogs of a mean age of 4 and 5 years, respectively. Dermoid cyst was also present in young dogs of a mean age of 4 years. Follicular cysts, which are reclassified in our study according to the new WHO classification into infundibular, sebaceous duct, isthmus, panfollicular cysts and

dialated pore, were observed at a mean age of 7 to 11 years, with the exception of the isthmus cyst, which seems to occur in young dogs at a mean age of 5 years.

Diag. 13: Age distribution of skin tumors, comparative diagram (dogs and cats)

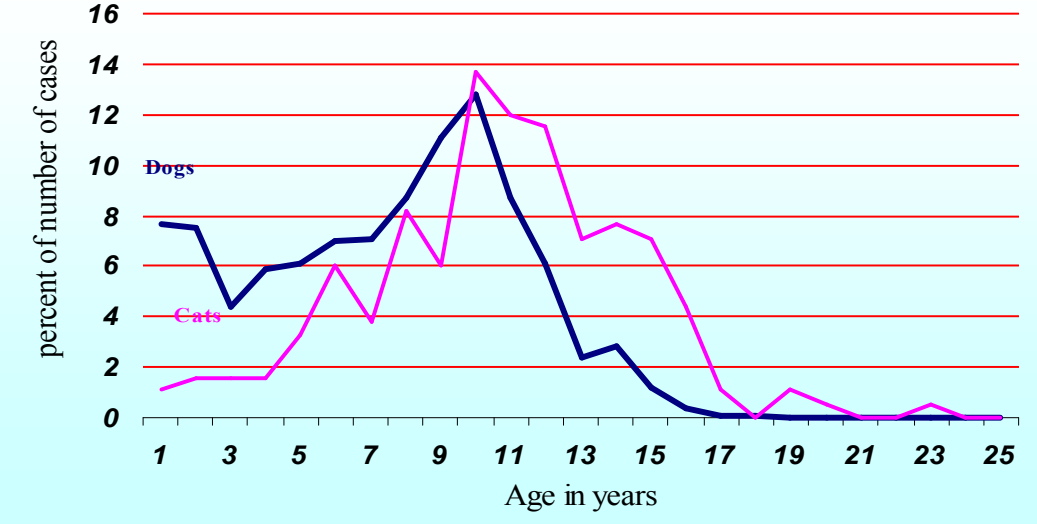


Diagram 13 shows the age distribution in both dogs and cats. The onset of the curves shows marked differences due to the histiocytoma in the dog. For both species the level is highest at the age of 10 years.

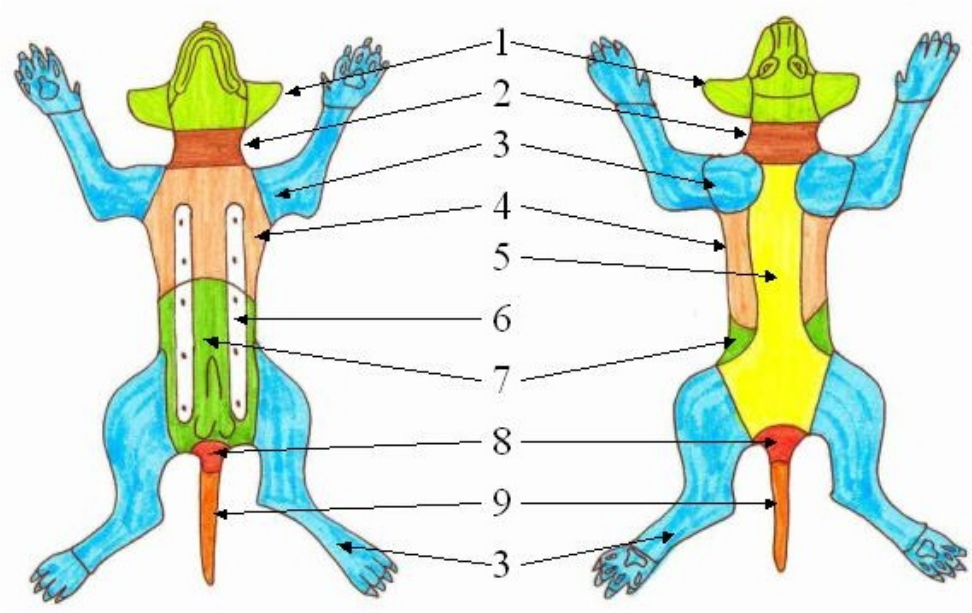
5.1.5. Sex distribution and predilection

Our collection shows a significant predominance of male dogs and cats. These results agree with the observations by Frese (1960) and Eskens (1983) regarding dogs, and were contrary to the observations by Goldschmidt and Shofer (1992) and Bomhard (2001) regarding dogs and cats.

In our study, many tumors and tumor-like lesions show sex predilection for male dogs and cats, however, this is more significant for trichoblastomas and basal cell tumors as well as all epitheliomas, and these findings will be discussed in detail below (see 5.3.1. and 5.3.5.). Apocrine ductal adenoma also shows a significant sex predilection for female dogs and cats and will be discussed in detail below (see 5.3.6.).

5.1.6. Anatomical location

The anatomical location of skin tumors is stated differently in the literature (Priester and Mckay, 1980, Goldschmidt and Shofer, 1992, Bomhard, 2001). A general division of the skin into head, neck, extremities, chest, back, abdomen, perianal, tail, and tumors without data was used by Bomhard (2001). In our work, we use this division with some modification. In our collection, we have about 20 tumors that were taken from the mammary gland region, and as they did not originate from mammary gland, we prefer to sort them under mammary gland region. Extremities are defined as limbs (arms and legs) (Pschyrembel, 2002) and we thus use the term in our thesis (Diagram 14).



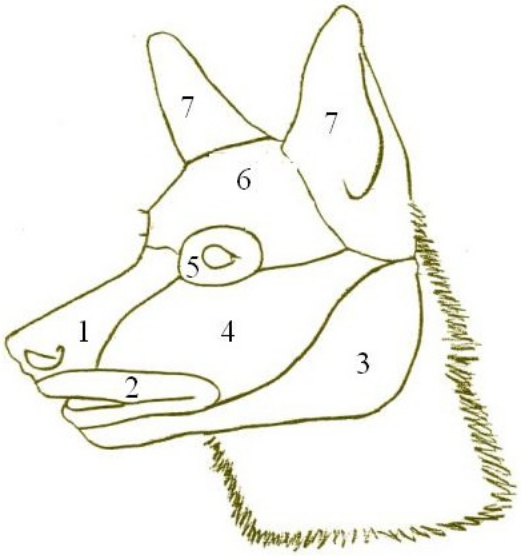
Diag. 14: Anatomical location: 1. Head, 2. Neck, 3. Limbs, 4. Chest, 5. Back, 6. Mammary region, 7. Abdomen, 8. Perianal, 9. Tail.

Head:

The superficial regions of the head are divided into regio paritalis, regio temporalis, regio frontalis, regio nasalis, regio infraorbitalis, regio zygomatica, regio orbitalis, regio oralis, regio mentum, regio buccalis, regio maxillaris, regio molaris, regio mandibularis, regio masseterica, regio parotidea and auricula (Popesko, 1997).

To facilitate our statistics and in accordance with the use of names in our field, we have used some abridged and modified terms for these regions, for example regio paritalis, regio temporalis, regio frontalis together are one location, namely regio infraorbitalis; regio zygomatica, regio maxillaris, regio molaris and part of regio masseterica together are named

cheek. Moreover regio mandibularis, part of regio masseterica, regio parotidea and mentum together are named mandibular region.



Diag. 15: Superficial regions of the head in a dog: 1. Nose, 2. Lips, 3. Mandibular region, 4. Cheek, 5. Eyelid, 6. Temporal, frontal and parietal regions, 7. Auricle. Modified from Popesko (1997)

In the literature (Gross et al., 1992, Goldschmidt and Shofer, 1992, Goldschmidt et al., 1998, Scott et al., 2001, Goldschmidt and Hendrick, 2002) as well as in our study, there are some tumors related to specific organs in the skin, which are found mainly in particular places on the body. These are anal sac tumors in perianal site, meibomian gland tumors on the inner aspect of the eyelid, ceruminous gland tumors in the ear canal, subungual keratoacanthoma and subungual squamous cell carcinoma which arise from the nailbed epithelium of the forelimbs or hindlimbs. Moreover, hepatoid gland tumors arise from hepatoid glands, which are located primarily at the perianal region, on the dorsal and ventral aspect of the tail, in the parapreputial area in males, at the abdominal mammary gland region in females, and can also be found in other locations (Goldschmidt and Shofer, 1992, Goldschmidt et al., 1998, Goldschmidt and Hendrick, 2002) such as the feet (Gross et al., 1992) and in one case in our study at the head. Thus, hepatoid glands are distinct anatomic entities closely related to sebaceous glands in their development (Isitor and Weinman, 1979).

Some skin cysts also relate to specific areas such as the subungual epithelial inclusion cyst, which is located within the bone of the third phalanx, and tumor-like lesions such as pressure point comedones, which are present primarily at the elbow (Goldschmidt et al., 1998).

Some other tumors and tumor-like lesions had no specific location at the skin, but they were located in one location more frequently than in others in the dogs in our collection. This group of tumors included the greater part of skin tumors and tumor-like lesions. These tumors were infundibular keratinizing acanthoma, which is commonly located at the back, trichoblastoma,

papilloma, apocrine ductal adenoma, sebaceous adenoma and epithelioma and melanomas, which are commonly located at the head. In addition, panfollicular and sebaceous duct cysts, sebaceous hyperplasia, fibroadnexal and follicular hamartomas, mast cell tumors, calcinosis circumscripta, canine hemangiopercytoma, fibroma and fibrosarcoma, were commonly located at the limbs, and apocrine adenoma and hemangiosarcoma at the neck.

In cats, squamous cell carcinoma, apocrine and melanocytic tumors were commonly found at the head and the auricle was the most common location of the squamous cell carcinoma. Trichoblastomas were commonly located at the limbs, and fibrosarcomas were found most often at injection (vaccination) sites (shoulder, between shoulder blades, chest wall and neck). Generally, the most common locations of skin tumors and tumor-like lesions in our study were the limbs and the head in both, dogs and cats.

5.2. Definition of the new terms in the new WHO classification

To avoid any mistake, we divide these tumors as follows:

Reclassified tumors:

Trichoblastomas were reclassified from basal cell tumors of the dog and cat because they originate in the hair germ of the developing follicle and not the basal cells (Goldschmidt and Hendrick, 2002). Sebaceous, meibomian and hepatoid epitheliomas were no longer classified as adenomas because they have a different prognosis as low malignant tumors. The newly classified sebaceous and meibomian ductal adenomas were separated from their previous classification as adenomas because of their origin in ductal epithelium. Squamous papilloma seceded from the old papilloma because it has no relation with viral infection and has a better prognosis (Goldschmidt et al., 1998, Goldschmidt and Hendrick, 2002). Some skin cysts such as isthmus, panfollicular and sebaceous ducts and the pressure point comedones were derived from the epidermoid cyst (Scott et al., 2001) and they are mentioned separately in the new WHO classification, probably due to their variable origin.

Renamed tumors:

In the new WHO classification many tumors are renamed, for example infundibular keratinizing acanthoma, pilomatricoma, infundibular cyst, fibroepithelial “polyp” and peripheral nerve sheath tumor (Goldschmidt et al., 1998), which were previously named intra-cutaneous cornifying epithelioma, necrotizing and calcifying epithelioma of Malherbe, epidermal cyst, cutaneous fibrous polyp and neurofibrosarcoma respectively (Weiss, 1974, Weiss and Frese, 1974); the reason is probably that these names were more descriptive of the origin of the lesions.

Newly discovered tumors:

Descriptions of these tumors were published in the period between the two WHO classifications, and they are mostly very rare tumors such as tricholemmoma (Diters and Goldschmidt, 1983, Walsh and Corapi, 1986), dilated pore (Scott and Flanders, 1984, Luther et al., 1989), ciliated cyst (Goldschmidt and Shofer, 1992), melanoacanthoma (Gross et al., 1992), nodular dermatofibrosis of the German shepherd dog (Lium and Moe, 1985, Moe and Lium, 1997), xanthoma (Fawcett et al, 1977, Gross et al., 1992), systemic (Moore, 1984), and malignant histiocytosis (Scott et al, 1979). Some lesions, as warty dyskeratoma, were new in the WHO classification, but the authors give no reference as to possible previous publications on these subjects (Goldschmidt et al., 1998).

Many subtypes or variants of different tumors had also been newly published, for example feline ventral abdominal angiosarcoma (Swayne et al., 1989).

Missdiagnosed tumors:

We suppose this group existed, but was always wrongly diagnosed, for example, subungual keratoacanthoma, which is similar to well-differentiated squamous cell carcinoma.

Collagenous hamartoma was probably previously identified as fibroma (Gross et al., 1992). Moreover, nodular fasciitis was probably missdiagnosed as fibrosarcoma because it has many clinical and histological features suggestive of a locally invasive fibrosarcoma as mentioned by Hendrick et al. (1998).

5.3. Skin tumors and tumor-like lesions in our cases

Under this heading we will discuss the skin tumors and tumor-like lesions investigated by us, individually and sometimes as groups that show definite characteristics or have been newly classified in the WHO classification.

5.3.1. Basal cell tumors and trichoblastomas (Fig. 2a-2x)

The term basal cell tumor has developed gradually in the history of the skin tumors of domestic animals. Its definition in the earlier literature was simple (Moultion, 1961), and it included trichoepithelioma as a subtype. Tumors which are now classified as trichoblastomas were described in the majority of the earlier publications as variants of basal cell tumors (Sedlmeier et al., 1967, Weiss and Frese, 1974, Stannard and Pulley, 1978, Seiler, 1982, Diters and Walsh, 1984, Madewell and Theilen, 1987, Pulley and Stannard, 1990, Yager and Wilcock, 1994), with only one exception, namely Gross et al. (1992), who defined and classified trichoblastomas separately. However, the new WHO classification by Goldschmidt

et al. (1998) reclassifies the majority of basal cell tumors of the dog and the spindle cell type of basal cell tumor of the cat as trichoblastomas and follows the classification by Gross et al. (1992). Sebaceous epithelioma, previously a variant of basal cell tumor (Yager and Wilcock, 1994), is classified under sebaceous gland tumors in the new WHO classification. Keratotic basal cell carcinoma, which was a type of basal cell tumor (Gross et al., 1992), is classified under tumors of epidermis as basosquamous carcinoma in the new WHO classification.

Canine basal cell tumor is an uncommon tumor according to the new WHO classification, and also in our study, where it constitutes 0.6 % (5 cases) of all skin tumors and tumor-like lesions. One of these cases was found at the perianal region and showed similarity to hepatoid gland epithelioma, because in one area it was mixed with hyperplastic hepatoid gland. However, because of the association with the overlying epidermis, the cystic degeneration and the presence of the hepatoid cells as masses in one area and not as individual cells, we diagnosed this case as a basal cell tumor (Fig. 2v-2x).

Feline basal cell tumor is considered to be common in the new WHO classification, and it is the third most common skin tumor in our study, with about 6 % of all skin tumors and tumor-like lesions. Basal cell tumors in the form of cystic variants were mentioned frequently in the literature (Diters and Walsh, 1984, Goldschmidt and Shofer, 1992, Goldschmidt and Hendrick, 2002), and 80% of basal cell tumors in the dogs and 73 % in the cats in our collection showed cystic degenerations.

Clear cell basal cell carcinoma is an uncommon tumor (Goldschmidt et al., 1998, Goldschmidt and Hendrick, 2002), which occurs more frequently in cats and can be differentiated from sebaceous carcinoma only with difficulty (Gross et al., 1992). In human medicine, this is an unusual variant of basal cell tumor (Barr et al., 1993) and must be differentiated from other clear cell tumors such as balloon cell malignant melanoma, granular cell tumors and sebaceous neoplasms (Kao et al., 1992). In some reports, the term granular (clear) cell basal cell carcinoma (Kao et al., 1992) or just granular cell basal cell carcinoma has been used (Dundr et al., 2004). However, clear cell basal cell carcinoma was not found in our collection, and the 3 cases of sebaceous carcinomas that were found in our collection (2 dogs and one cat) were histologically easy diagnosed without confusion with clear cell basal cell carcinoma.

Trichoblastomas appear mostly as basal cell tumors in the literature (Madewell and Theilen, 1987, Goldschmidt and Shofer, 1992, Bomhard, 2001, Goldschmidt and Hendrick, 2002) and

they are mentioned as a separate category only by Gross et al. (1992). According to these publications, trichoblastomas have no marked sex predilection. However, the majority of trichoblastomas and basal cell tumors were found in males in both, dogs and cats of our collection. This finding was more obvious with regard to trichoblastomas, in dogs as well as in cats (Table 39).

Tab. 39: Basal cell tumors and trichoblastomas in dogs and cats

	Dog			*Cat*		
	n	♂ %	♀ %	n	♂ %	♀ %
Basal cell tumor	5	80	20	11	64	36
Trichoblastoma	16	69	31	9	89	11
Total/ Means	21	74.5	25.5	20	76.5	23.5

The total numbers and the mean percentages in table (35) reflect the results for basal cell tumors according to the old WHO classification.

Gross et al. (1992) mentioned that the prevalence of trichoblastomas in dogs was very close to the prevalence of basal cell tumors, which ranged from 3 % to 12 %, although it was difficult to estimate in cats because many other tumors such as apocrine ductal neoplasms and neoplasms of epidermal basal cell origin had been involved in the feline basal cell tumors (Gross et al., 1992). In spite of our search, we did not find any study carried out mainly on trichoblastomas. However, we describe here 16 cases of canine trichoblastomas and 9 cases of feline trichoblastomas. The prevalence of feline trichoblastomas (4.6 %) exceeded canine trichoblastomas (2 %). Trichoblastomas were found mostly at the head of dogs (60%), whereas it was more common at limbs of cats (67 %) in our study, while Goldschmidt and Hendrick (2002) mention that head and neck were the primary sites of occurrence of trichoblastomas in the dog and cat, and Scott et al. (2001) mention that lesions in cats occur most commonly on the cranial half of the trunk.

There is no clear breed predilection in trichoblastomas, but the most common dogs were German shepherd dog and Westhighland white terrier. Ribbon type trichoblastoma was the most common variant (88 %) in the dogs in our collection, while trabecular was the most common variant (67 %) in the cats. Trichoblastomas seem to occur in young and old dogs from one to 14 years, with a mean age of 8 years, while it is a tumor of old cats between 6 and 15 years, with a mean age of 11 years. In comparison with basal cell tumors in our study, we note that basal cell tumor is a tumor of aged dogs and cats of mean ages of 10 and 13 years, respectively.

5.3.1.1. Granular cell trichoblastoma (Fig. 2i-2l)

This variant is very rare and only few cases have been described in dogs and rats (Seiler, 1981, Courtney et al., 1992, Yoshitomi and Boorman, 1994). In our case as well as in the previously published cases (Seiler, 1981, Courtney et al., 1992, Yoshitomi and Boorman, 1994), the tumor contains two different types of cells, basaloid cells and granular cells. All cases in dogs, including our case, showed mixed form, ribbon type and granular cell foci. The presence of the basaloid cells is the key to identify this kind of tumors easily, and according to our search, no any pure granular cell trichoblastoma was reported. Therefore we suppose that many pure granular cell trichblastomas might be miss-diagnosed as other granular cell tumors.

In all the previous cases, including a similar case of granular cell basal cell tumor in human (Dundr et al., 2004), the tumor cells contained a varying amount of PAS positive granules. However, the nature of the cytoplasmic eosenophilic granules was considered to be secondary lysosomes (Seiler, 1981, Courtney et al., 1992, Yoshitomi and Boorman, 1994, Dundr et al., 2004). Immunohistological technique was done in the human case and confirmed the lysosomal nature of the cytoplasmic granules by the expression of CD68 antigen, which is a glycoprotein associated with lysosomal membranes (Dundr et al., 2004). We applied for the first time an immunohistological technique on canine granular cell trichoblastoma. Ribbon and granular cells were expressed Cytokeratin and were negative for Vimentin, which confirmed the epithelial nature. A human case of granular cell basal cell carcinoma of the skin was reported with immunocytochemical positivity for lysozyme (Bosccaino et al., 1997), however, our case was negative lysozyme immunohistology. Additionally, S100 demonstration was performed to exclude a granular cell tumor which is presumptively of Schwann cell origin (Hendrick et al., 1998).

In conclusion, granular cell trichoblastoma is a rare epithelial tumor and can be easily diagnosed in the mixed cases with appearance of basaloid cells arranged in ribbons, otherwise, immunohistological techniques, especially the demonstration of Cytokeratin expression should be helpful for differentiation.

5.3.1.2. Clear cell trichoblastomas (Fig. 2m- 2q)

The development of adnexa is the result of intimate interaction between basal cells and mesenchymal cells. The basal cells become the germinative cells of the hair follicle that will give rise to the specialized components of the follicle, the hair shaft, the internal root sheath, and the external root sheath as well as, in the case of these tumors, to trichoblastomas

(Goldschmidt et al., 1998). Of these, the clear cell differentiation in our cases resembles a differentiation similar to the lower part of the external root sheath which itself is composed of cells that have a very pale cytoplasm and rich with glycogen. This part of the external root sheath can develop to the inferior type of a tricholemmoma that is characterized by islands of neoplastic cells with pale cytoplasm and central cells that have more abundent eosinophilic cytoplasm. The islands in tricholemmoma are surrounded by a prominent basal lamina zone that is positive in the periodic acid-Schiff reaction (PAS) and shows blue staining with the Masson's trichrome stain (Diters and Goldschmidt, 1983, Walsh and Corapi, 1986). These features that are found in tricholemmoma were found in some areas in our cases. These features together with the presence of the PAS-positive cytoplasmic granules support the hypothesis that the cells in our cases showed differentiation towards the lower part of the external root sheath of the hair follicle. However, the significant population of small, trichoblastic (basaloid) epithelial cells helps differentiate this tumor from a tricholemmoma. In the only reported case of a human clear cell trichoblastma, however, no PAS positivity was mentioned. The author discussed lysosomal degenerative changes as cause of the clear cell morphology (Tronnier, 2001).

The presence of the tumor cells near the base of a hair follicle in one of our cases may represent the origin of this tumor from the hair follicle.

Sebaceous differentiation was found in our cases in form of scattered large cells that are similar to sebocytes. Normally, the sebaceous gland develops from a bulge at the superficial portion of an invaginated cord of epithelial cells that formed a hair follicle (Goldschmidt et al., 1998). Therefore, sebaceous and external root sheath differentiation in our cases may represent that trichoblasts have the ability to differentiate to the external sheath of the hair follicle as well as their adnexa, and we consider, that an apocrine differentiation which mentioned in some cases of human trichoblastmas (Usmani et al., 2002, Yu et al., 2005) might be occur in animals.

Generally, the tumors described here showed a growth pattern similar to that of ribbon trichoblastoma but consisted mainly of clear cells, some basaloid cells and scattered sebaceous cells. Additionally, few nests of outer root sheath differentiation similar to inferior (bulb) tricholemmoma (i.e. thick basement membrane zone, PAS positivity, peripheral palisading of epithelial cells, central eosinophilic cells) were found.

Because of the dominance of the clear cells in the described tumors, we prefer to use the term clear cell trichoblastoma in tumors which show the described features.

5.3.1.3. Cystic variant of trichoblastoma (Fig. 2r-2u)

Cystic degeneration is common in basal cell tumors according to the litrature (Joeger, 1988, Miller et al., 1991, Goldschmidt and Hendrick, 2002), and this feature is mentioned as a central caseation necrosis in basal cell carcinoma and is not described in benign feline basal cell tumors (Gross et al., 1992, Scott et al., 2001). In our collection, 80% of basal cell tumors in dogs and 73 % in cats showed this feature, while only two cases of trichoblastoma showed this manifestation; these were one single case of ribbon and one of trabicular variant in cats. Because they were two cases out of 9 feline trichoblastomas in our collection (1 % of all feline skin tumors and tumor-like lesions), we assume that the cystic variant of trichoblastoma is common in cat, rare, or does not occur at all in dogs. In addition, the presence of this feature in trichoblastomas may be disproving that this feature related to basal cell carcinoma as mentioned by some authors (Gross et al., 1992, Scott et al., 2001).

5.3.1.4. Malignant trichoblastoma

Malignant trichoblastomas are not mentioned in the new WHO classification of tumors of domestic animals, but were first described by Mikaelian and Wong (2003) who described follicular stem cell carcinomas with metastasis, lymphatic invasion and necrosis in dogs.

Neoplasms of follicular stem cells would reasonably be expected to resemble trichoblastomas and basal cell carcinomas, therefore, this publication was criticized by the authors themselves (Mikaelian and Wong, 2004) and by Walder (2005); they urge that this neoplasm be referred to as clear cell or balloon-cell sweat gland carcinoma. So far, we support the view, on the basis of the above description, that trichoblastomas are benign tumors in animals despite the fact that in human pathology, malignant trichoblastic carcinomas have frequently been reported (Rofagha et al., 2001, Kazakov et al., 2004).

5.3.2. Other follicular tumors (Fig. 1a-1e, 2e-2u)

This group comprises many new tumors and new nomenclatures of the new WHO classification. It includes infundibular keratinizing acanthoma, tricholemmoma, trichoepithelioma and pilomatricoma in addition to trichoblastoma which was discussed above (see 5.3.1.) (Goldschmidt et al., 1998, Goldschmidt and Hendrick, 2002). Only trichoepithelioma and pilomatricoma (under the name necrotizing and calcifying epithelioma of Malherbe) were classified under follicular tumors, while infundibular keratinizing acanthoma was classified separately and not as hair follicle tumor in the old WHO classification.

In our study, generally speaking, this group of tumors was more common in dogs (72 cases with 8.8 % prevalence) than in cats (10 cases with 5.0% prevalence). Trichoepithelioma and infundibular keratinizing acanthoma were the more common follicular tumor (31 % and 26 %, respectively). Trichoblastoma and pilomatricoma were also common, with 22 % and 19 % of the follicular tumors in dogs. Malignant follicular tumors were noticed only in one case of malignant trichoepithelioma, and therefore malignant follicular tumors seem to be uncommon skin tumors in dogs.

These tumors are commonly located at the back, with the exception of trichoblastomas, which, in our study, are located more commonly on the head. The location at the back of infundibular keratinizing acanthoma was in agreement with the results of Abramo et al. (1999), while the other follicular tumors in our study differed from the results of that study.

Regarding cats, two types of follicular tumors were found in our collection, namely 9 cases of trichoblastoma and one case of trichoepithelioma.

5.3.2.1. Infundibular keratinizing acanthoma

A common canine follicular tumor in our study was classified separately in the old WHO classification and was not classified as hair follicle tumor, as it is in the new one (Weiss and Frese, 1974, Goldschmidt et al., 1998). This tumor was designated keratoacanthoma in the U.S.A., but this name was not accepted in the old WHO classification (Weiss and Frese, 1974). According to the new WHO classification, the diagnosis of keratoacanthoma should be reserved for tumors of subungual origin (Goldschmidt et al., 1998), and two cases of subungual keratoacanthoma in our study will be discussed under nailbed tumors (see 5.3.3.2.).

The cyst with epithelial proliferation was considered an early stage of infundibular keratinizing acanthoma in the old WHO classification (Weiss and Frese, 1974); however, no lesion resembling this stage of infundibular keratinizing acanthoma was found in our collection.

The tendency of infundibular keratinizing acanthoma to occur in male dogs, as mentioned by Stannard and Pulley (1975), was not supported by our study. The mean age in the literature so far and in our study differed slightly; it was 5.3 years in Stannard and Pulley (1975), 6 years in Abramo et al. (1999), 7.3 years in Goldschmidt and Shofer (1992) and 8 years in our study. We therefore consider infundibular keratinizing acanthoma a tumor of young adult dogs. The back was the most common location of infundibular keratinizing acanthoma as many authors have found (Stannard and Pulley, 1975, Abramo et al. (1999), and so have we in our study. However, the limbs were the second most common predilection sites in our study, and they

are mentioned as the most common location by Goldschmidt and Shofer (1992). Norwegian elkhounds were predisposed (Yager and Wilcock, 1994, Goldschmidt and Shofer, 1992, Goldschmidt and Hendrick, 2002), but Norwegian elkhound was not observed in our collection, and no clear breed predilection was observed.

5.3.2.2. Tricholemmoma

This tumor has been newly classified in the WHO classification, and only few cases have been reported in dogs (Diters and Goldschmidt, 1983, Walsh and Corapi, 1986). Trichilemmal carcinomas in man have frequently been reported (Allee et al., 2003, Lai et al., 2003), but no cases in animals. However, tricholemmoma is not found in our study and seems to be rare.

5.3.2.3. Trichoblastoma

A detailed discussion of this tumor is found above (see 5.3.1.).

5.3.2.4. Trichoepithelioma

It was the most common follicular skin tumor of dogs in our study. The back has been described as the most common predilection site by many authors (Madewell and Theilen, 1987, Gross et al., 1992) as well as in our study. However, the limbs have been mentioned as the more common location by Goldschmidt and Shofer (1992), and additional other locations as neck and thorax have also been mentioned (Abramo et al., 1999, Goldschmidt and Hendrick, 2002). The tumor is more commonly present in young adult dogs according to most of the literature (Gross et al., 1992, Goldschmidt and Shofer, 1992, Abramo et al., 1999, Goldschmidt and Hendrick, 2002) and this has been confirmed by our study. Breed predilection for Munsterlaender was observed in our study, while Basset hound had an increased disposition as Goldschmidt and Hendrick (2002) have found. Trichoepithelioma shows slightly increased tendency to occur in female dogs in our results, which agrees with the findings of Goldschmidt and Shofer (1992).

Dogs with malignant trichoepithelioma and metastasis in lymph node and lung have been reported (Sells and Conroy, 1976). One case in our study was diagnosed as a malignant trichoepithelioma because of its histological appearance, but no other masses or metastases were mentioned in the case history of the affected dog.

A single case of trichoepithelioma was found at the shoulder of a 9-year-old male ESH cat in our collection, however, this tumor is uncommon in the cat and no breed or sex predilection have been reported (Goldschmidt and Hendrick, 2002).

5.3.2.5. Pilomatricoma

This is a common canine follicular skin tumor that occurs relatively more frequently in younger dogs than other follicular skin tumors, as has been found in our collection and by other authors (Gross et al 1992, Goldschmidt and Shofer, 1992, Abramo et al., 1999, Goldschmidt and Hendrick, 2002). According to existing literature, Kerry blue terriers had the highest risk (Madewell and Theilen, 1987, Gross et al 1992, Goldschmidt and Shofer, 1992, Goldschmidt and Hendrick, 2002). In our study, however, just two Kerry blue terriers were found in the whole collection, and they had other kinds of skin lesions (one fibrosarcoma and one sebaceous hyperplasia); in our collection, Airedale terriers had the highest disposition for pilomatricoma. A clear sex predilection was observed in our collection (64 % female dogs), of which nothing is found in the aforementioned literature. Back and limbs were the most common locations in our study, but different locations were reported in the above literature.
An aggressive malignant tumor with metastasis in bone, lung and lymph nodes was reported (Rodriguez et al., 1995), but no characteristics of malignancy were seen in the 14 cases of pilomatricomas in our collection.

5.3.2.6. Trichofolliculomas

These are rare benign neoplasms in dogs and cats (Gross et al., 1992, Scott et al., 2001), while they are the most common skin tumors in guinea pigs and represent 45 % of all their skin tumors (Frank and Frese, 1988). These neoplasms are considered to be highly structured hamartomas of the pilosebaceous unit (Gross et al., 1992, Scott et al., 2001) and they were classified as skin hamartomas in human pathology (Ackerman et al., 1993). The term trichofolliculoma does not appear in the new WHO classification, therefore, we assume this lesion was classified as fibroadnexal or follicular hamartoma or it may be missing in the new WHO classification. The lesions that were diagnosed as hamartomas in our collection were very simple and could not be confused with the trichofolliculoma mentioned in the previous literature, and we therefore have reported that trichofolliculoma was not found in our collection and might be a rare lesion in dogs and cats.

5.3.3. Tumors of the epidermis and nailbed tumors (Fig. 4a-4d)

5.3.3.1. Tumors of the epidermis

This group of tumors includes papilloma (papillomatosis) and inverted papilloma as benign tumors (Campbell et al., 1988, Shimada et al., 1993). Actinic keratosis (Hargis and

Thomassen 1979), multicentric squamous cell carcinoma in situ or bowen-like disease (Baer and Helton, 1993), squamous cell carcinoma and basosquamous carcinoma represent the malignant tumors (Goldschmidt et al., 1998).

Inverted papilloma and actinic keratosis were not observed in our collection and seem to be rare.

5.3.3.1.1. Squamous cell carcinoma

5.3.3.1.1.1. Dog

The prevalence of squamous cell carcinoma varies between 1.7 % and 7.25 % in the literature (Frese, 1960, Eskens, 1983, Goldschmidt and Shofer, 1992, Bomhard, 2001) and it constitutes 3 % of all skin tumors and tumor-like lesions in our study. However, according to the new WHO classification, squamous cell carcinomas represent 0.9 % of all skin tumors and tumor-like lesions and seem to be uncommon in our study, although this tumor was reported as a common skin tumor in the new WHO classification (Goldschmidt et al., 1998). In contrast, subungual squamous cell carcinomas, which are listed under the common skin tumors, were observed in 2.1 % of all skin tumors and tumor-like lesions and seem to be common in our study as well as in the new WHO classification (Goldschmidt et al., 1998). Both types of squamous cell carcinomas show a marked tendency to occur in females, i.e. 67 % of squamous cell carcinoma and 61 % of subungual squamous cell carcinoma. This sex predilection agrees with the results of Goldschmidt and Shofer, (1992), but contradicts the results of Frese, (1960) and Bomhard (2001). A tendency of squamous cell carcinoma towards Schnauzer was reported by Goldschmidt and Hendrick (2002) and Bomhard (2001), but note that the results of Bomhard (2001) did not include the subungual squamous cell carcinoma and that means that these results may not reflect the tendency of squamous cell carcinoma precisely. However, in our study this tendency was shown only by the subungual tumor, while no clear tendency was observed in the other one. No difference in the mean age was observed between the two kinds of squamous cell carcinomas, which was 9 years, and that was in agreement with Bomhard's findings (2001).

The acantholytic and spindle cell squamous cell carcinoma reported by Goldschmidt et al. (1998) and Goldschmidt and Hendrick (2002) and the signet-ring squamous cell carcinoma reported by Espinosa et al. (2003) were not found in our collection and seem to be rare.

5.3.3.1.1.1. Cat

Squamous cell carcinoma was the most common epithelial skin tumor in the cat and represented 8.6 % of all skin tumors and tumor-like lesions in our study. 12 tumors out of 17 were located at the head (mostly at auricle (70%) and eyelids (20%)). In most cases, ESH cats were affected. Our results partially agreed with those found in the literature (Goldschmidt and Shofer, 1992, Goldschmidt et al., 1998, Bomhard, 2001, Goldschmidt and Hendrick, 2002), with the exception that squamous cell carcinoma was the second most common epithelial tumor after basal cell tumor according to Bomhard (2001) and the third after basal and mast cell tumors according to Goldschmidt and Shofer (1992). The preponderance of basal cell tumors as the common epithelial skin tumor could be explained by the old WHO classification approach in these publications (Goldschmidt and Shofer, 1992, Bomhard, 2001) (see 5.3.1).

5.3.3.1.2. Basosquamous carcinoma (Fig. 5d)

This tumor was classified in the old WHO classification as a variant of basal cell tumor (Weiss and Frese, 1974) and considered as an epidermal tumor in the new WHO classification. No sex predilection has been noted by Goldschmidt and Hendrick (2002); in our study also, it was found in males in 63% out of 8 cases of basosquamous carcinoma. This finding may be related to the participation of the basaloid cells, which was observed in many other tumors in our study such as basal cell tumors, trichoblastomas and epitheliomas. No clear breed predilection was noted in our results, whereas Goldschmidt and Hendrick (2002) mention that Scotch terrier was at increased risk. Abdomen and limbs were the most common sites of basosquamous carcinoma in our study, while head and neck are mentioned by Goldschmidt and Hendrick (2002). This tumor was not found in cats in our collection and is not mentioned in cats in the literature (Goldschmidt et al., 1998, Goldschmidt and Hendrick, 2002).

5.3.3.1.3. Papilloma

Papilloma is caused by infection with a papillomavirus (Shimada et al., 1993) and should be distinguished from a squamous papilloma (see 2.5.1.7.1., table 1 and 8.3.3.). In our collection, 50% of all papillomas that were diagnosed according to the old WHO classification (Weiss and Frese, 1974) were reclassified as squamous papillomas and are discussed under tumor-like lesions (see 5.3.8.). However, the other 50% were classified as viral papillomas, which represented 1 % of all skin tumors and tumor-like lesions in the dog, and were seen at

different ages, but more common in young dogs. They were found more commonly on the head especially on the lips with no marked breed predilection.

Papillomas are uncommon in the dog and the cat according to Goldschmidt and Hendrick (2002), but they are relatively common in dogs and not found in the cats in our study.

5.3.3.1.4. Multicentric squamous cell carcinoma in situ (Fig. 5a-5c)

This is a form of carcinoma in situ which is considered to be uncommon in cats and rare in dogs by Scott et al. (2001), and in our study was found in a single case in a dog and in a cat, respectively. This tumor may progress to invade through the basement membrane and should then be classified as squamous cell carcinoma (Goldschmidt et al., 1998). The case of the cat in our study showed invasion of the tumor cells in the external root sheath of hair follicles, and in some areas the tumor edges were not sharp, therefore, we used an immunohistological technique (cytokeratin) to show the edges of the tumor and to confirm that no single cell invasion was present in this case.

5.3.3.2. Nailbed tumors

Gross et al. (1992) and Marino et al. (1995) have reported that larger dogs showed more digit masses than dogs of less weight. In 19 cases out of 117, digit masses (16 %) were subungual squamous cell carcinomas (Marino et al., 1995) and 9 from 21 canine nailbed epithelial neoplasms were subungual keratoacanthomas (Walder and Barr, 1984). These data suggest that benign neoplasms may be as common as malignant neoplasms of the nailbed. Subungual keratoacanthoma was not mentioned in the study of Marino et al. (1995) probably because this tumor was previously diagnosed as well-differentiated subungual squamous cell carcinoma (Gross et al., 1992, Yager and Wilcock, 1994).

In our study, 20 cases out of 91 with digit masses (22 %) were nailbed tumors, represented by 18 subungual squamous cell carcinomas and two subungual keratoacanthomas. Breed predilection of subungual keratoacanthoma is not mentioned by Goldschmidt et al. (1998) or Goldschmidt and Hendrick (2002), while Gross et al. (1992) state that no apparent breed predilection was found with regard to the affected dogs. However, this group of tumors generally shows a clear tendency towards some dog breeds in our results. Subungual keratoacanthoma was found only in two Standard schnauzer dogs. 50% of subungual squamous cell carcinomas were found in Schnauzer dogs (5 Standard schnauzer, 2 of each giant schnauzer and Schnauzer {breed not further specified}), and two cases were found in Scotch terrier.

The tendency of subungual squamous cell carcinoma to affect Giant schnauzer and Standard schnauzer was reported by Bomhard (2001) and Goldschmidt and Hendrick (2002).

In spite of the small number of the subungual keratoacanthoma in our collection, and because of the above results, we consider that all nailbed tumors may have the same breed predilection, and the most common skin tumors in Standard schnauzer are nailbed tumors (see below). Because of the similarity between subungual keratoacanthoma and subungual squamous cell carcinoma and to avoid misdiagnosis, we compare both tumors in view of existing literature and of our results in order to facilitate accurate diagnosis (table 40).

Tab. 40: Comparison between keratoacanthoma and well-differentiated squamous cell carcinoma

Feature	*Keratoacanthoma*	*well-differentiated squamous cell carcinoma*
Basaloid layer in proliferating endophytic lobules*	Yes	Variable; often none
Penetration of basal lamina by neoplastic cells**	No	May occur
Nature of keratotic plug*	Often orthokeratotic	Often parakeratotic
Cellular necrosis*	Infrequent	Often present
Glassy cytoplasm*	Always	Variable
Glycogen content (PAS)***	High and regular	Variable and irregular
Cup-shaped architecture*	Usually	Variable
Central keratine core***	Usually	No
Bone lyses***	May occur	May occur
Bone invasion***	No	Common
Single cell invasion of stroma*	Only pseudoinvasion at periphery	May be present
Breed predilection****	Standard schnauzer	Standard schnauzer, Giant schnauzer, Schnauzer (breed not further specified), and Scotch terrier

*Murphy (1991), **Goldschmidt and Hendrick (2002), ***Gross et al. (1992), **** Our result

Tumors in Standard schnauzer dogs:

In our study were included 11 Standard schnauzer dogs with 12 tumors and tumor-like lesions, 7 of which were nailbed tumors (58 %), 5 subungual squamous cell carcinomas, two subungual keratoacanthomas and one case of papilloma at the paw. The other tumors were single cases of hepatoid gland adenoma at the perianal region, meibomian adenoma at the eyelid, sebaceous adenoma at the back and apocrine cyst at the chest. Therefore, we report that the main location of the tumors in this dog breed is paw (67 %), especially the subungual region. There was no possibility to compare our results because we did not find any study performed on and limited to the tumors in Standard schnauzer dogs.

5.3.4. Cysts (Fig. 6a-6f)

Epidermal cyst has been classified in both WHO classifications and in our collection was the most common cyst in dogs and cats, and it is also named infundibular, epidermoid and epidermal inclusion cyst (Goldschmidt et al., 1998). In the old WHO classification, the majority of cutaneous cysts were follicular cysts (Weiss and Frese, 1974). Follicular cysts could be further categorized by the level of the follicle from which they develop as infundibular, isthmus, matrical and panfollicular cysts (Scott et al., 2001). In the above classification, infundibular cyst is part of the follicular cysts, while the old WHO classification described epidermal and follicular cysts separately, and in the new WHO classification, infundibular cyst is classified as epidermal cyst. Therefore, we could consider that infundibular cyst constituted a considerable part of both, the old follicular and new epidermal cysts. According to the division of follicular cysts by Weiss and Frese, (1974), Scott et al. (2001) and according to our understanding, follicular cysts in the new WHO classification were divided into infundibular, sebaceous duct, isthmus, panfollicular cysts and dialated pore. The infundibular cyst of the new WHO classification also includes epidermal cysts, probably because both look identical.

Subungual epithelial inclusion cyst was reported under the tumors of bones and joints in the old WHO classification (Misdorp and Heul, 1976) and was the most common skin cyst type of the toe in dogs (63 %) (Frank et al., 1995). Our work showed a similar result with 4 skin cysts at toe in dogs, 2 of which were subungual epithelial inclusion cysts, the others werd one apocrine cyst and one sebaceous duct cyst.

Apocrine and dermoid cysts have been classified in both WHO classifications and have been reported without any change.

Generally, according to our results, skin cysts were common in the dog (10%) and occupied the third place among the skin tumors and tumor-like lesions after those with adnexal differentiation and histiocytic tumors. The most common skin cysts in dogs were infundibular (44 %), apocrine (21 %), panfollicular (10%) and sebaceous duct cysts (10%). Isthmus, dermoid (5 % each) and subungual epithelial inclusion cysts (2 %) were uncommon cysts.

Dermoid cyst and follicular cyst were considered to be more common in young animals (Bomhard, 2001). In our study, dermoid cyst was present also in young dogs of a mean age of 4 years. Infundibular, sebaceous duct, isthmus, panfollicular cysts and dialated pore, were observed at a mean age of 7 to 11 years, excluding isthmus cyst, which seemed to occur in younger dogs at a mean age of 5 years.

In cats, skin cysts were also common (1.5 %) but less than in dogs, and the most common cyst was infundibular cyst, which represents the only cyst type that was found in our collection (3 cases). Other cysts such as ciliated cyst and dialated pore were not present in our collection and seem to be rare.

Many other kinds of skin cysts have been reported in animals, especially in dogs and cats, but are not presented in the new WHO classification, despite the fact that they were reported in the time before the new WHO classification. These cysts were matrical cyst (Gross et al., 1992), cysts with precarcinomatous epithelial transformation (Frese and Weiss, 1969) and branchial cyst (Karbe and Nielsen, 1965, Smith and Gunson, 1977, Clark and Kostolich, 1989, Hance and Robertson, 1992, France et al., 2000, Scott et al., 2001). These cysts were not found in our collection and seem to be rare.

5.3.5. Sebaceous and modified sebaceous tumors

This group was very common in dogs and less common in cats according to our results as well as the literature (Stiglmair-Herb, 1987, Yager and Wilcock, 1994, Goldschmidt and Shofer, 1992, Weiss and Teifke, 1999, Scott et al., 2001, Goldschmidt and Hendrick, 2002). In the dog, it was found mainly at the head with the exception of hepatoid gland tumors, which were found mainly at the perianal region.

Sex predilection varied between above publications. In our study, these tumors were found more frequently in males than females, with exception of meibomian adenoma and carcinoma, which occured mostly in females.

Sebaceous ductal adenoma (Fig. 8c-8d)

Among the 98 sebaceous and modified sebaceous gland tumors in the dogs of our collection, no sebaceous ductal adenoma was observed. However, among only 4 sebaceous and modified sebaceous gland tumors in cats in our collection, we found two (50%) sebaceous ductal adenomas.

This tumor was newly classified, and the new WHO classification (Goldschmidt et al., 1998) is the only source which mentions that this tumor is common in dogs, uncommon in cats and rare in other animals. From our results, and in spite of the small sample, we consider that sebaceous ductal adenoma in cats is the common sebaceous and modified sebaceous gland tumor and is rare in dogs.

Epitheliomas (Fig. 8a-8b)

According to our search, there has been no study that discusses epitheliomas separately from the related tumors. Goldschmidt and Hendrick (2002) mentioned that sebaceous and meibomian tumors have no sex predilection, but hepatoid gland tumors have a marked sex predilection toward males. In our study, we found 12 epitheliomas (5 sebaceous, 5 hepatoid gland and two meibomian) in dog, all of them found in male dogs (100%). Epitheliomas histologically showed a preponderance of basaloid reserve cells, and may have marked mitotic activity, little nuclear atypia with a variable degree of melanization and scattered well-differentiatd cells (Goldschmidt et al., 1998). This histologic appearance of these basaloid cells is similar in many ways to the cells in basal cell tumor and trichoblastoma. With the above results for basal cell tumors and trichoblastomas, we consider that these basaloid cells are closely related as to their origin, and they have a tendency to occur in males rather than in females.

Canine breeds that are predisposed to the formation of epitheliomas include Newfoundlands and huskies (17 % each).

These tumors are of low grade malignancy in a small proportion of cases, but especially those arising from sebaceous gland on the head may show metastasis to the mandibular lymph nodes (Goldschmidt and Hendrick, 2002). This metastatic phenomenon was not noticed in our cases.

Hepatoid gland angioadenoma and angioepithelioma (Fig. 8e-8f)

Weiss and Frese (1974) subdivided hepatoid gland adenomas into adenomas with secondary vascularization and adenomas with transitional cell forms, which is more common. The second has been classified in the new WHO classification as hepatoid gland epithelioma according to our comparison of the histological appearances, while the former subtype is not mentioned in the new WHO classification. Weiss and Frese (1974) have described those hepatoid gland adenomas with vascularization, and mention that they are characterized by large glandular areas with small vessels and islands of soft tissue surrounded by reserve cells, and they recurred more frequently than others; and this was by comparison with the hepatoid gland epithelioma that is described in the new WHO classification as a tumor of low-grade malignancy. Goldschmidt and Hendrick (2002) describe that some hepatoid gland adenomas showed extremely ectatic vessels within the interlobular stroma and the term “secondary vascularization” was not used in that publication.

In our study, we found this vascularization phenomenon in 9 out of 44 hepatoid gland adenomas (20%) and in 4 out of 5 hepatoid gland epitheliomas (80%), and the sex, age and breed division was the same as in the main group. We recommend using the terms hepatoid gland angioadenoma and angioepithelioma to define these variants and we suggest more research to evaluate their roll in the recurrence of these tumors.

5.3.6. Apocrine and modified apocrine tumors

These tumors were more common in cats (18 %) than in dogs (3%); the percentages refer to all skin tumors and tumor-like lesions in our study. These results did not agree with those reported by some authors (Scott et al., 2001, Goldschmidt and Hendrick, 2002), but agreed with those mentioned by Goldschmidt and Shofer (1992). Ceruminous gland tumors were found only in cats in our study, and most of them were malignant (87.5 %).

Apocrine ductal adenoma and carcinoma

Apocrine ductal adenoma was named papillary syringadenoma in the old WHO classification (Weiss and Frese, 1974).

Apocrine ductal adenoma and carcinoma are reported separately from the other related adenomas and carcinomas by Goldschmidt and Shofer (1992), and Weiss and Frese (1974). Eskens (1983) and Bomhard (2001) do not mention these ductal tumors, which might be represented under apocrine adenoma and carcinoma. Goldschmidt and Shofer (1992) found that apocrine ductal adenoma was the less common apocrine tumor in dogs and cats. However, according to our results, apocrine ductal adenoma was a more common apocrine tumor in the dog (30%), and occurred commonly on the head (57 %) of females (71 %), while there were fewer apocrine adenoma and apocrine carcinoma in the cat, and they occurred commonly on the head (75 %) of females (75 %).

5.3.7. Hamartomas (Fig. 7a-7c)

This is a newly classified group which was not mentioned in the old WHO classification. Hamartomas are circumscribed congenital lesions of the skin, characterized by hyperplasia of one or more skin components, and are commonly reported in dogs and cats (Scott et al., 2001). The term Hamartoma rather than the term naevus has been chosen in the new WHO classification to describe these lesions, in order to avoid any possible confusion with the melanocytic nevi in humans (Goldschmidt et al., 1998). Despite this new nomenclature, some authors still used the term nevi (Scott et al., 2001). Hamartomas are subclassified into

epidermal (pigmented epidermal naevus), follicular, sebaceous, apocrine and fibroadnexal hamartomas (adnexal naevus, focal adnexal dysplasia, folliculosebaceous hamartoma) (Goldschmidt et al., 1998). Yager and Wilcock (1994) mention many of these lesions. They use the term fibroadnexal dysplasias for fibroadnexal hamartomas, among them the so-called giant hair follicle disease or organoid naevus that seems in many ways similar to follicular hamartoma of our recommendation.

13 collagenous hamartomas were diagnosed in our collection and have been discussed also under tumors of fibrous tissue (see 5.3.10.).

According to our results, hamartomas in dogs (epithelial and mesenchymal) amount to 4.2 % and represent the ninth most common skin lesion of all skin tumors and tumor-like lesions in dogs, with a slight inclination toward females (53 %) and more common at the limbs (52 %). The more common hamartomas in dogs were collagenous (38 %), follicular (26 %) and fibroadnexal hamartomas (23 %). Sebaceous hamartoma was less common (11 %) and the apocrine hamartoma seems to be uncommon. Epidermal hamartoma was not found in our collection, and we consider it as rare hamartoma.

Hamartomas are found in young and old dogs, perhaps because the animal owner overlooked them at an early age, or they are not only congenital lesions.

Hamartomas were less common in cats (1 %) than in dogs (3 %); there were only two follicular hamartomas, which seem to be the more common hamartomas in old cats.

5.3.8. Tumor-like lesions (Fig. 3c-3d)

Not all tumor-like lesions have been included in this group in the new WHO classification, and this term covers only some epithelial skin lesions. They are different lesions and the only thing they have in common is that they are no tumors. This group took the sixth place among the skin tumors and tumor-like lesion in the dog in our collection.

Sebaceous hyperplasia was the most common tumor-like lesion and represented 2.8 % of all skin tumors and tumor-like lesion in the dogs in our collection. This result agreed with the result of Goldschmidt and Shofer (1992). However, Eskens (1983) mentioned that sebaceous hyperplasia represented about 6 % of all skin tumors and tumor-like lesions. The slight inclination to females as mentioned by Goldschmidt and Shofer (1992) was also found in our collection (52 %). This inclination contradicted the findings of Weiss and Frese (1974) and Madewell and Theilen (1987). Limbs and head were the more common location in our study, and aged animals were more affected as has also been reported by other authors (Gross etal., 1992, Goldschmidt and Shofer, 1992, Scott et al., 2001).

Sebaceous hyperplasia was the only tumor-like lesion found in the cats of our collection, which may be due to the small number of cats in our study.

Fibropruritic nodule was the second most common tumor-like lesion in the dogs of our collection, and it seems to be more common in male dogs (64 %), with no clear breed predilection. Limbs and back were the more common location of this lesion. All cases found at the limbs (40%) are by preference named acral lick granulomas as described by Goldschmidt et al. (1998). However, the presence of the lesion at the back (30%) raises questions as to the cause for the arising and development of the lesion.

Fibroepithelial polyp (Weiss, 1974) was a common lesion in dogs in our collection; it was named cutaneous fibrous polyp in the old WHO classification, where it was classified as mesenchymal lesion. It has been classified under epithelial lesion in the new WHO classification (Goldschmidt et al., 1998), probably, because of the exophytic appearance of the lesion and the share of the hyperplastic epidermis. This lesion seems to be one of old dogs, more common in females (75 %) and found mostly at the limbs and back according to our results.

Squamous papilloma was also a common lesion in the dogs in our collection, which was seen in animals of different ages, but more commonly in young dogs. It is found more commonly on the limbs and the head with no marked breed predilection. This lesion is distinguished from a viral papilloma by many histological differences as shown in table 1 (see 2.5.1.7.1.) and figures 3a-3d (see 8.3.3).

Pressure point comedone was an uncommon lesion in the dog in our collection (a single case). This lesion showed similarity to skin cysts, and we did not see any reason to classify it under tumor-like lesions rather than under skin cysts.

Cutaneous horn and warty dyskeratoma were not found in our collection and seem to be rare lesions in dogs and cats.

5.3.9. Melanocytic tumors and tumor-like lesions

This group with 5.3 % of the tumor and tumor-like lesion groups in dogs took the eighth place in our study, but with 1.5 % it was uncommon in cats; the head was the most common location in both species. Older dogs had more malignant melanomas than younger dogs, and it was vice versa with regard to melanocytomas. Melanocytomas inclined toward males (60%) rather than toward females, while malignant melanomas inclined to females (55 %) rather than males, with no clear breed predilection.

Subungual malignant melanoma is a relatively common digital neoplasm in the dog (Goldschmidt et al., 1998). It was present in 7 cases, i.e. about 32 % of all malignant skin melanomas in the dogs in our study. However, the cases of subungual malignant melanoma represented 87.5 % of all subungual melanomas, while melanocytoma (benign melanoma) was present in only one case, which is 12.5 % of all subungual melanomas.

Melanoacanthoma was not found in our collection. The tumor synonymes are not mentioned in the new WHO classification. In order to perform literature research, synonymes like melanocytoma-acanthoma were needed, because this tumor was published only under this synonyme (Gross et al., 1992, Espinosa et al., 2000). We therefore recommend stating all the synonymes, as far as possible, behind the respective tumors to facilitate search with regard to these tumors.

Naevus has only been described as a human lesion and is not classified as a skin lesion of animals in the new WHO classifications. The term naevus is defined as a birthmark (Goldschmidt et al., 1998), and it is commonly used for describing pigmented melanocytic lesions of the epidermis and dermis in humans and is not used in veterinary dermatopathology (Smith et al., 2002). The old WHO classification described comparable conditions, which seemed to exist only in dogs and pigs (Weiss and Frese, 1974). Many pigmented skin lesions of dogs were comparable to a certain degree with human naevus. Among these, canine melanocytomas with junctional activity resemble the human compound naevus, some of the canine dermal melanocytomas resemble the blue naevus and canine epidermal hyperpigmentation (melanocytic hyperplasia) resembles naevus spili. Conditions comparable to the human junction naevus were not reported (Kraft and Frese, 1976b). This term (naevus) has not been accepted in the new WHO classification. However, melanocytic hyperplasia is mentioned as a newly classified skin lesion under the melanocytic tumors. It was first described in dogs by Kraft and Frese (1976a), and has been reported in orange and silver shorthair cats (Nash and Paulsen, 1990, Nesbitt, 1998, Scott et al., 2001). In an investigation of the necropsy of 594 dogs carried out by Kraft and Frese (1976b), 52 dogs had 244 lesions of circumscribed epidermal hyperpigmentation, and in 26 dogs 43 lesions of a lentigo-like proliferation of teat epithelium were recorded. These results did not agree with our results because no melanocytic-like lesions were found in dogs and cats in our collection, and the reason might be that these lesions looked harmless and were not operated. Therefore they are considered to be rare in the biopsy work and may be more common in the necropsy work if they are more often taken into consideration.

5.3.10. Tumors of fibrous tissue

This group was the most common in cats with 40.0% and less common in dogs with 7.5 % of all the skin tumors and tumor-like lesions in our study. Malignant tumors were fibrosarcoma and myxosarcoma, which were present in both animals. However, they were more dominant in cats and represented 99 %, while in dogs they represented 60% of all fibrous tumors in our study. Fibrosarcoma was the most common skin tumor in cats in our study as well as in most of the literature (Stiglmair-Herb, 1987, Jorger, 1988, Goldschmidt and Shofer, 1992, Goldschmidt and Hendrick, 2002). However, it was less common than basal cell tumor, mast cell tumor and squamous cell carcinoma in another study (Miller et al., 1991). In the above publications, the prevalence of this tumor varied between 14.7 % and 43.9 %, and our prevalence was 37.6 %. This variation in the prevalence may be related to the differences in the vaccination programs implemented at the times and the places of these studies. In our study, the back was the most common location of feline fibrosarcomas followed by limbs and chest. Head and extrimities were the most common locations as reported by Goldschmidt and Hendrick (2002) while trunk and extrimities are mentioned by Gross et al. (1992).

Fibromas have been mentioned as uncommon lesions in dogs and cats (Gross et al., 1992, Scott et al., 2001), however, they were most often seen in the dog in our study and also by Goldschmidt and Hendrick (2002). They have been reported in the cat (Gross et al., 1992, Scott et al., 2001, Goldschmidt and Hendrick, 2002), but some investigators believe that feline tumors that have the histological appearance of fibromas are actually well differentiated fibrosarcomas (Goldschmidt and Shofer, 1992). We therefore consider that this may be the reason for the absence of fibroma in cats in our results.

Myxomas and myxosarcomas were rare and observed in middle-aged or older dogs and cats (Goldschmidt and Shofer, 1992, Gross et al., 1992, Goldschmidt and Hendrick, 2002). Myxomas in dogs and cats were rarely reported (Marolt et al., 1973, Machida et al., 2003) and in our study we found only a single case each in a dog and a cat. One other case in a dog showed empty areas, and was immunohistologically positive for vimentin and factor VIII-related antigen. We therefore prefer to classify this case as an atypical myxoma or angiomyxoma. However, myxosarcomas, which we found in 5 dogs and 4 cats, seem to be more common than myxomas.

We diagnosed 13 skin lesions as collagenous hamartomas according to the new WHO classification. Some investigators (Goldschmidt and Shofer, 1992) suggest that the term fibroma should be used rather than collagenous hamartoma, as it conforms to the standardized nomenclature of soft tissue tumors in domestic animals published in the old WHO

classfication. Location, size, pattern cellularity and growth form were used to reach an accurate diagnosis (Gross et al., 1992, Wilcock and Yager, 1994) as in table 2 (see 2.5.2.1.1.2.) and figures 9a-9e (see 8.3.9.). These lesions were discussed above under hamartomas.

Feline sarcoid is a newly reported rare neoplasm (Rest et al., 1997, Gumbrell et al., 1998, Schulman et al., 2001, Scott et al., 2001, Hanna and Dunn, 2003, Teifke et al., 2003) whose histological appearance resembles the equine sarcoid (Scott et al., 2001). Feline sarcoid was recently reported and is not found in either WHO classification; it was not observed in our collection.

The newly classified malignant fibrous histiocytoma (Hendrick et al., 1998) as well as its benign variant in dogs (Scott et al., 2001) were not observed in our collection and considered to be rare.

However, malignant fibrous histiocytoma in the cat is one histologic variant of postvaccinal sarcomas (Hendrick et al., 1998). Malignant fibrous histiocytoma and fibrosarcomas made up the majority of the postvaccinal sarcomas. Histologically, there was much overlap between fibrosarcomas with giant cells and malignant fibrous histiocytoma (Hendrick and Brooks, 1994), therefore, all these tumors were classified as fibrosarcomas in our study.

5.3.11. Tumors of adipose tissue

Lipoma in dogs was found more commonly in females in our collection (63 %) as well as in some publications (Goldschmidt and Shofer, 1992, Bomhard, 2001), in contrast to the results of Frese (1960). In our collection, no clear breed predilection was noticed and the affected dogs were of middle and older ages. Chest was the most common place followed by limbs and abdomen.

In our study, lipoma in cats was found more commonly in males (60%) and this was in agreement with the result of Goldschmidt and Shofer (1992). Limbs and back were the most common location and the affected cats were of middle and older ages.

The infiltrative lipoma is a newly added variant (McChesney et al. 1980, Bergman et al., 1994, Hendrick et al., 1998) that is uncommon in dogs and rare in cats (Gross et al., 1992). In our study, two cases were found in dogs, and none was found in cats.

Liposarcomas, its well-differentiated, pleomorphic and myxoid variants (Weiss, 1974, Messick and Radin, 1989, Hendrick et al., 1998), the newly classified angiolipoma (Hendrick et al., 1998, Liggett et al., 2002) and the other lipomas, which are not mentioned in the new WHO classification but were reported as myxoid lipoma (Weiss, 1974), fibrolipoma (Gross et

al., 1992), chondrolipoma (Goldschmidt and Shofer, 1992), intermuscular lipomas (Thomson et al., 1999), and pigmented lipoma (Scott et al., 2001) were not found in our collection and considerd to be rare.

5.3.12. Tumors of muscle

Tumors of muscle include leiomyoma, leiomyosarcoma, rhabdomyoma and rhabdomyosarcoma (Weiss, 1974, Hendrick et al., 1998). Other variants, as fibroleiomyoma (Hendrick et al., 1998, Liu and Mikaelian, 2003), angioleiomyoma, angioleiomyosarcoma (Liu and Mikaelian, 2003) and embryonal rhabdomyosarcoma of the urinary bladder or botryoid sarcoma or sarcoma botryoides (Kuwamura et al., 1998, Takiguchi et al., 2002) were also reported. However, cutaneous tumors of smooth and striated muscles are extremely rare in dogs and cats in the veterinary literature (Roth, 1990, Goldschmidt and Shofer, 1992, Scott et al., 2001, Goldschmidt and Hendrick, 2002). In our collection, only one case of leiomyosarcoma was found at neck of 11-years-old male Cocker spaniel dog, and it was verified immunohistologically by demonstration of vimentin and smooth muscle actin.

5.3.13. Tumors of vascular tissue

Tumors of vascular tissue included hemangioma, lymphangioma, hemangiosarcoma, lymphangiosarcoma and scrotal vascular hamartoma (Weiss, 1974, Hendrick et al., 1998). Other lesions, as Kaposi-like vascular tumor, angiokeratoma, epithelioid haemangioendothelioma and a lesion that was similar to cutaneous bovine angiomatosis have also been reported in dogs (Yager and Wilcock, 1994, Hendrick et al., 1998, Machida et al., 1998, Vala and Esteves, 2001, Goldschmidt and Hendrick, 2002, Vincek et al., 2004, Kim et al., 2005). In our results, hemangioma and hemangiosarcomas showed breed predilection for German shepherd dogs (31 %) and showed higher prevalence in male (63 %) than female in this breed compared to other breeds.

We have not found any study that describes and discusses the sex and breed predilection of cutaneous hemangioma and hemangiosarcomas of the skin for the German shepherd dog. However, such predilection is mentioned by other authors for these tumors when occurring in internal organs (Appleby, 1991, Goldschmidt and Hendrick, 2002).

One case of feline ventral abdominal angiosarcoma was found in our collection. Instead of the term feline ventral abdominal angiosarcoma, we prefer to use the term feline ventral abdominal lymphangiosarcoma, because this origin of the tumor was confirmed by Swayne et al. (1989) and Galeotti et al. (2004). However, this tumor seems to be uncommon in the cats,

while Kaposi-like vascular tumor, lymphangioma, angiokeratoma, epithelioid haemangio-endothelioma, scrotal vascular hamartoma and cutaneous angiomatosis were not found in our study and seem to be rare in both dogs and cats.

5.3.14. Tumors of peripheral nerves, synovium and mesothelium

In dogs, malignant peripheral nerve sheath tumor and hemangiopericytomas have very similar histomorphologic features, and because of this similarity, the true prevalence of this tumor was unknown (Goldschmidt and Hendrick, 2002). In our study, we diagnosed two cases of malignant nerve sheath tumor in male dogs. From the immunohistological results as in table 23 (see 4.1.8.15.), hemangiopericytoma and leiomyosarcoma could be not excluded in these cases if compared with that mentioned by Chijiwa et al. (2004), who reported additionally that the positivity with nerve growth factor receptor and the negativity with α-smooth muscle actin might be helpful for differentiating canine peripheral nerve sheath tumors from other sarcomas including rhabdomyosarcomas and canine hemangiopricytomas. However nerve growth factor receptor was not demonstrated in our work, but the presence of the nerve remnant in one case and the similarity of the histological appearance in both cases with that mentioned in the literature, i.e., the arrangement of the cells in small interwoven bundles (Hendrick et al., 1998, Goldschmidt and Hendrick, 2002) and the presence of spindle-shaped cells that exhibit nuclear palisading (Scott et al., 2001), combined with the expression of some immunohistological stains, especially GFAP and NSE, were enough to arrive at our diagnoses (Fig. 10a-10f). However, all hemangiopericytomas in our study were diagnosed only histologically because they appeared more typical to those reported in the literature (Hendrick et al., 1998, Goldschmidt and Hendrick, 2002). According to our results, tumors of peripheral nerves seem to be uncommon in dogs.

According to the new WHO classification, the tumors of synovium consisted of synovial sarcoma only. Primary tumors of synovium are uncommon in the dog; however, synovial sarcomas occur most frequently in the stifle joint (Harasen, 2002) and appear to be more common in males than females (Pool and Thompson, 2002). In a recent study by Craig et al. (2002), more than 51 % of the intra-articular tumors were histiocytic sarcomas, while only 14 % were recognized as synovial cell sarcomas. In addition, the authors hypothesized that intra-articular histiocytic sarcoma arises from the dendritic cells found within the inflamed synovium associated with degenerative joint disease (Craig et al., 2002). However, two synovial sarcomas were found in two male dogs in our study, which supports the inclination

to male dogs that is mentioned by Pool and Thompson (2002) and were found in knee joint and toe and not in the stifle joint. According to our results, tumors of synovium seem to be uncommon in dogs.

In cats, malignant peripheral nerve sheath tumor has been rarely reported (Summers et al., 1995), and there is very little information about synovial tumors in cats in the literature (Silva-Krott et al., 1993, Pool and Thompson, 2002), however, Silva-Krott et al. (1993) state that most reported synovial cell tumors in cats were benign, and they report one case of synovial sarcoma at the cubital joint of a 9 year old male shorthair cat. In our study we observed no case of peripheral nerves and synovium tumors and therefore, they seem to be rare in cats.

Tumors of mesothelium are classified under many organs in the new WHO classification, in skin and soft tissues (Hendrick et al., 1998), alimentary (Head et al., 2003), and respiratory system (Dungworth et al., 1999). Mesothelioma is the only tumor that has been mentioned in this group (Hendrick et al., 1998). It has been reported in dogs and cats (Head et al., 2002). However, no case of mesothelioma was found in dogs and cats in our collection, therefore, it seems to be rare in both, dogs and cats.

Granular cell tumor:

Granular cell tumor has been reported in dogs and cats (Patnaik, 1993) and is mentioned under tumors of peripheral nerves in the new WHO classification, because it has a presumptive Schwann cell origin (Hendrick et al., 1998). Some other authors mention this tumor as a neoplasm of uncertain origin (Cooper and Valentine, 2002). In our study we observed not any case of granular cell tumor and therefore, it seems to be rare in both dogs and cats.

5.3.15. Mast cell tumors

Canine mast cell tumor was the most common mesenchymal cutaneous neoplasm of dogs in the old WHO classification, while histiocytoma is the most common canine skin tumor in the new WHO classification (Weiss, 1974, Hendrick et al., 1998). In our study, canine mast cell tumor was placed in the second place with 6.9 % of all the skin tumors and tumor-like lesions after canine cutaneous histiocytoma. It is a malignant tumor and its biological behavior correlates with the histological grade (Hendrick et al., 1998, Goldschmidt and Hendrick,

2002). In our collection, we observed a gradual reduction in the percentages from grade I to grade III, which were 45, 39, and 16 % of grade I, II and III respectively. Most tumors occurred in middle-aged dogs and had no sex predilection. Boxer was the most common breed in our collection as well as in the literature (Madewell and Theilen, 1987, Goldschmidt and Shofer, 1992, Yager and Wilcock, 1994, Scott et al., 2001).

In our study as well as in studies by other authors (Madewell and Theilen, 1987, Goldschmidt and Shofer, 1992, Goldschmidt and Hendrick, 2002), feline mast cell tumors are less common than in dogs. This tumor was represented in the tenth place with 3 % of all skin tumors and tumor-like lesions in cats in our collection. No sex predilection was found, and two out of 6 cases were found in Persian cats in our collection. However, Scott et al. (2001) and Goldschmidt and Hendrick (2002) mentioned that Siamese cats had a higher risk of developing mast cell tumors.

Feline mast cell tumor is mostly a benign tumor (Hendrick et al., 1998) and the prevalence of behaviourally malignant tumors was reported in about 2 % of the cases (Wilcock et al., 1986, Miller et al., 1991). Many cats with mast cell tumors will develop additional tumors, which do not occur at the site of previous surgery, but at sites distant from the primary tumor (Goldschmidt and Shofer, 1992). Mitotic activity seems to be the most effective prognostic tool for feline cutaneous mast cell tumor (Johnson et al., 2002, Lepri et al., 2003), and therefore we used only the mitotic activity to determine the malignancy of mast cell tumors in the cat histologically. We found only one case (almost 17 %) out of 6 cutaneous feline mast cell tumors that showed a high mitotic rate (3 to 5 per high power field of 40X), and one cat with a benign mast cell tumor showed additionally a lipoma.

Feline histiocytic mast cell tumor variant (Hendrick et al., 1998) and the newly reported pleomorphic cutaneous mast cell tumor (Johnson et al., 2002) were not found in our collection and seem to be rare variants.

5.3.16. Histiocytic tumors

In our collection, these tumors were found commonly in dogs and no case was found in cats. Generally, histiocytic tumors are mainly canine tumors as is shown in most of the literature (Eskens, 1983, Goldschmidt and Shofer, 1992, Gross et al., 1992, Yager and Wilcock, 1994, Hendrick et al., 1998, Bomhard, 2001, Goldschmidt and Hendrick, 2002), however, few cases were reported in other animals such as cat, horse and cattle (Sutton and McLennan, 1987, Gafner and Bestetti, 1988, Court et al., 1993, Lester et al., 1993, Walton et al., 1997). Three cases of malignant histiocytomas were reported in cats. They represented 0.21 % of all the

feline skin tumors reported by Bomhard (2001) as in table 43 (see 8.1.), and we think that the author has used the term malignant histiocytoma as a synonyme of malignant histiocytosis. Canine cutaneous histiocytoma, which is named benign round cell sarcoma by Frese (1960) (Weiss and Frese, 1974), was the most common skin tumor type in most of the literature (Eskens, 1983, Goldschmidt and Shofer, 1992, Gross et al., 1992, Yager and Wilcock, 1994, Hendrick et al., 1998, Bomhard, 2001, Goldschmidt and Hendrick, 2002), with a standardised incidence rate of 337 per 100,000 dogs per year (Dobson et al., 2002). It was also the most common skin tumor in our study with 16.2 % of all skin tumors and tumor-like lesions. They were found to be more common on the head, with an inclination to male dogs (67 %) and with breed predilection for Dobermann, Boxer and Golden retriever, which is also mentioned by Goldschmidt and Hendrick (2002). Only three cases of cutaneous histiocytosis were found in male dogs in our collection and therefore it seems to be uncommon, while xanthoma and systemic histiocytosis were not found and seem to be rare.

Terminologically, malignant histiocytosis, a newly classified tumor, was not found in the old WHO classification (Weiss, 1974, Hendrick et al., 1998). Scott et al. (1979) reported one case of lymphoreticular neoplasia in a dog resembling malignant histiocytosis in humans and described this tumor similar to that found in the old WHO classification as histiocytic lymphosarcoma (Jarrett and Mackey, 1974). This tumor, which is mentioned in the old WHO classification, had unknown origin and was classified under lymphosarcoma only due to the anatomical distribution, which was similar to lymphosarcoma. These tumors, according to Scott et al. (1979) and Jarrett and Mackey (1974), in many ways resemble the malignant histiocytosis that is found in the new WHO classification. However, the multinucleated cells that are often present in large numbers, as is mentioned in the new WHO classification, are not described. Multinucleated large cells have been mentioned in many studies (Moore and Rosin, 1986, Hayden, 1993, Ramsey et al., 1996), but only the presence of binucleated cells was mentioned by Jarrett and Mackey (1974) and Scott et al (1979). We consider that malignant histiocytosis was the same tumor that was mentioned in the old WHO classification as histiocytic lymphosarcoma. However, in our study, all 4 cases were found in middle-aged Bernese mountain dogs (6 to 8 years), three females and one male. Three were located at limbs and one at the chest. This tumor seems to be uncommon and constitutes about 0.5 % of all skin tumors and tumor-like lesions in the dog. However, it was found in 16 % of all Bernese mountain dogs that occurred in our collection.

5.3.17. Calcinosis circumscripta

Generally, calcinosis circumscripta is more common in the skin than in other locations such as the oral cavity and intestine (Tafti et al., 2005). It was described by some authors only in dogs (Weiss, 1974, Hendrick et al., 1998) and by others also in cats (Scott et al., 2001, Head et al, 2002).

In our collection, we found this tumor in 13 dogs with 1.6 % of the all skin tumors and tumor-like lesions; therefore, this lesion seems to be common in dogs and rare in cats. The ages of dogs ranged from one to 6 years, and the majority (67 %) were under two years of age, and this was in agreement with Gross et al. (1992). Most of the affected dogs were German shepherd and Rottweiler dogs in our collection and also in that of Tafti et al. (2005).

Multicentric periarticular calcinosis:

Calcinosis circumscripta is described as an identical lesion to tumoral calcinosis in humans in the new WHO classification. This was not accepted by Pool and Thompson (2002), who preferred to use the term multicentric periarticular calcinosis in animal for a lesion which seems to be like tumoral calcinosis in humans. Periarticular location distinguishes multicentric periarticular calcinosis from calcinosis circumscripta (Pool and Thompson, 2002). Therefore only three lesions (23 %) out of 13 cases of calcinosis circumscripta in our collection should be regarded as multicentric periarticular calcinosis. These cases were located on two elbows and one tarsal joint of young dogs less than 2-years-old.

5.3.18. Hemangiopericytoma

In the new WHO classification, this tumor is still brought under “unclassified tumors” (Hendrick et al., 1998) in spite of the ultrastructural and immunohistochemical confirmation of its pericytic origin (Xu, 1986, Perez, 1996, Mazzei et al., 2002). According to this evidence and the histological appearance of this tumor, we recommend classifying it under vascular tumors.

Hemangiopericytoma in animal occurs mainly in the skin of dogs (Goldschmidt and Hendrick, 2002, Mazzei et al., 2002), however, some primary noncutaneous lesions as spleen (Mazzei et al., 2002) and liver (Cullen and Popp, 2002) have been reported. Predilection for location on the limbs was observed in our study and also by Gross et al. (1992), Goldschmidt and Hendrick (2002) and Mazzei et al. (2002); this refers to almost 74 % of all hemangiopericytomas in our study. This tumor was common in dogs with 2.3 % of all skin tumors and tumor-like lesions in our study, and had no clear sex or breed predilection.

5.4. Classification problems of some skin lesions according to the new WHO classification

Altogether, 37 of the skin lesions found in our collection, 25 in dogs and 12 in cats, were excluded because we followed the new WHO classification. In dogs, these were 8 lymphosarcomas, 5 extramedullary plasmocytomas, 4 which could not be classified, three meibomian gland hyperplasias, two chondrosarcomas, one osteosarcoma, one hepatoid gland hyperplasia and one anal sac gland hyperplasia.

In cats, these were 4 extramedullary plasmocytomas, 4 lymphosarcomas, three which could not be classified and one meibomian gland hyperplasia.

Lymphosarcomas and extramedullary plasmocytomas have been classified under hematopoietic tumors (Valli et al., 2002), chondrosarcomas and osteosarcomas under bone and joint tumors (Slayter et al., 1994). Moreover, hepatoid gland hyperplasias have been classified under tumors of the alimentary system (Head et al., 2003), while the tumors that could not be classified, meibomian gland hyperplasias and anal sac gland hyperplasias are not found in the new WHO classification.

5.5. Other skin tumors that are not found in the new WHO classification

The new WHO classifications of the skin and soft tissue tumors in domestic animals were published in 1998. In the period of 8 years since then, many new skin tumors and tumor variants have been described in animals. For example, feline sarcoid (Scott et al., 2001, Schulman et al., 2001, Teifke et al., 2003) has also been reported frequently as a cutaneous fibropapilloma in the cat (Gumbrell et al., 1998, Schulman et al., 2001, Hanna and Dunn, 2003). In addition, pigmented cutaneous papillomatosis or pigmented epidermal hamartomas have been reported (Tanabe et al., 2000, Narama et al., 2005). Another variant of squamous cell carcionoma has been described as signet-ring squamous cell carcinoma (Espinosa et al., 2003) and histiocytic sarcoma has been classified by some authors (Scott et al., 2001, Affolter and Moore, 2002). Furthermor a benign variant of malignant fibrous histiocytoma has been described in dogs and cats (Scott et al., 2001) and cutaneous histiocytosis has also been reported (Affolter and Moore, 2000). Arrector pili hamartoma, angioleiomyoma and angioleiomyosarcoma have recently been reported in dogs and cats (Liu and Mikaelian, 2003). Another variant of mast cell tumor named pleomorphic cutaneous mast cell tumor has been newly reported in the cat (Johnson et al., 2002). Cutaneous canine angiomatosis that is

similar to cutaneous bovine angiomatosis has been recently reported (Kim et al., 2005). The clear cell trichoblastoma and cystic trichoblastoma are newly mentioned variants in our study. Some other variants mentioned by other authors or found in the old WHO classification are not mentioned in the new WHO classification, such as many variants of lipomas, namely, myxoid lipoma (Weiss, 1974), fibrolipoma (Gross et al., 1992), chondrolipoma (Goldschmidt and Shofer, 1992), intermuscular (Thomson et al., 1999) and pigmented lipomas (Scott et al., 2001), and angiokeratoma (Yager and Wilcock, 1994, Vala and Esteves, 2001).

6. SUMMARY

A new or second edition of the international histological classification of skin, melanocytic and soft tissue tumors of domestic animals was published in 1998 with new entities and some new nomenclatures. For the period since then, we have not found a statistical study that discusses all these tumors in relation to the new WHO classification. Therefore, it has been the aim of this study to apply the new WHO classification in the epidemiology of the skin tumor entity.

A statistical analysis of canine and feline skin tumors and tumor-like lesions was carried out using the diagnostic material of the Institute for Veterinary Pathology, Justus-Liebig-Universitaet Giessen, Germany. These comprised 816 skin tumors and tumor-like lesions in 768 dogs, and 197 skin tumors and tumor-like lesions in 194 cats. These lesions were classified according to the recommended WHO nomenclature and classification of tumors in domestic animals. Evaluation of the distribution of breed, age, sex, location and the tumor types was done in comparison with the prevalence of the same tumor in the literature.

More than 25 % of the dogs in our collection were Mongrels, and the five most common breeds that were found in our collection were German shepherd dog, Boxer, Golden retriever, Westhighland white terrier and Cocker spaniel.
The number of breeds in cats was less than in dogs, and the most common breed was Mongrel cats. The mean age of the skin tumor carriers in our collection was 7.5 years in dogs and 10.6 years in cats. The dominant skin tumor origin was epithelial with 49.3 %, while tumors of mesenchymal origin were 45.3 % and of melanocytic origin 5.3 % of all skin tumors and tumor-like lesion in dogs. In cats, the mesnchymal tumors were always the dominant group with 54.0%, followed by the epithelial tumors with 40.5 % and the melanocytic tumors with 1.5 % of all skin tumors and tumor-like lesions. The general sex distribution in dogs was 56.4 % male and 43.6 % female, while it was 55.5 % males and 44.5 % females in cats. The most common locations of the skin tumors and tumor-like lesions were limbs and head in both, dogs and cats.

In our collection, 62 tumor types were found in the dog. The 10 most common skin tumors and tumor-like lesions in dogs were canine cutaneous histiocytoma, mast cell tumor, lipoma,

hepatoid gland adenoma, infundibular cyst, fibrosarcoma, sebaceous hyperplasia, malignant melanoma, trichoepithelioma and melanocytomas, consecutively. 31 tumor types were found in the cat. The 10 most common skin tumors and tumor-like lesions in cats were fibrosarcoma, squamous cell carcinoma, apocrine adenoma, basal cell tumor, lipoma, trichoblastoma, ceruminous gland carcinoma, hemangiosarcoma, apocrine carcinoma and feline mast cell tumor, in this order.

In our study, we have described for the first time the clear cell and cystic variants of trichoblastoma and reported the immunohistological expression of the canine granular cell trichoblastoma, which so far had been reported neither in the literature nor in the WHO classifications.

We have discussed some other tumors and tumor-like lesions that are found in the literature and have not been classified in the new WHO classification.

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8. APPENDIX

8.1. Tables

Tab. 41: Prevalence of skin tumors and tumor-like lesions in dogs by different authors

Tumor	*Frese (1960) (n=389)(%)*	*Eskens (1983) (n=4507)(%)*	*Goldschmidt and Shofer (1992)(%)*	*Bomhard (2001) (n=47008)(%)*
Basal cell tumor	2	5.84	3.7	5.9
Basal cell carcinoma			0.3	0.01
Basosquamous carcinoma			0.3	
Papilloma	2.75	0.09	0.3	1.41
Squamous cell papilloma		0.62		
Fibropapilloma		0.51		
Squamous cell carcinoma	7.25	2.31	1.7	2.97
Sebaceous adenoma	4.25	4.66	4.1	7.29
Sebaceous carcinoma		0.27	0.7	0.11
Hepatoid gland adenoma	17.75	9.19	9.2	5.91
Hepatoid gland carcinoma		2.24	0.3	0.15
Meibomian gland adenoma			3.1	
Meibomian gland carcinoma			0.3	
Apocrine adenoma, (Syringoma)*, (papillary apocrine adenoma)**, (Hidradenoma)****	0.25	0.31	1.7	1.36
Apocrine ductal adenoma			0.3	
Cystadenoma		0.22		
Spiradenoma		0.13		
Apocrine mixed tumor**		0.29		
Fibrocystadenoma	0.25			
Fibroadenoma papilliform	0.5			
Adenoma	2			
Apocrine carcinoma (papillary)**		0.44	0.7	0.06
Apocrine carcinoma (tubular)**		0.27		
Apocrine carcinoma (solid)**		0.44		
Apocrine malignant mixed tumor**		0.18		
Carcinoma	3.5			
Adenocarcinoma	3			
Ceruminal gland adenoma		0.22	0.3	0.03
Ceruminal gland mixed tumor		0.02		
Ceruminal gland carcinoma		0.27	0.3	0.1
Anal sac gland carcinoma			0.7	0.46
Trichoepithelioma		3.17	4.1	2.6
Epithelioma Malherbe	0.5	1.66	1.0	3.98
Unclassified epithelioma		0.09		
Intracutaneous cornifying epithelioma	1.5	1.91	1.7	2.25
Benign melanoma	5.5	4.19	3.2	4.12
Malignant melanoma	5.5	1.18	0.8	1.94
Fibroma	4	1.26	1.9	1.82
Fibromyxoma		0.09		
Myxoma (Myxomatous tumors)***	0.25		0.5	
Myxolipoma		0.02		
Hemangiopericytoma			6.8	
Fibrosarcoma	3.75	5.19	1.5	7.9
Fibromyxosarcoma		0.11		
Lipoma	2.5	3.08	7.8	6.22
Liposarcoma	0.25	0.24	0.5	0.21
Hemangioma	3.75	2.95	4.4	3.09
Perithelioma	0.25			
Lymphangioma	0.25	0.02	0.5	
Hemangiosarcoma (Angiosarcoma)*	0.25	0.75	1.0	1.29
Leiomyoma (Myoma)*	0.25	0.09		0.14

Continue tab. 41

Tumor	*Frese (1960) (n=389)(%)*	*Eskens (1983) (n=4507)(%)*	*Goldschmidt and Shofer (1992)(%)*	*Bomhard (2001) (n=47008)(%)*
Leiomyosarcoma				0.01
Neurofibroma				0.1
Neurofibrosarcoma				0,02
Neural tumors			0.5	
Mast cell tumor(not metastatic)**	6.5	10.12	9.7	7.99
Metastatic mast cell tumor		0.16		
Malignant lymphoma	0.25	0.24	1.0	0.52
Retothel sarcoma	0.25			
Mycosis fungoides				0.24
Extramedullary plasmocytoma			1.5	1.37
Histicytoma (benign round cell sarcoma)*	7.25	11.54	11.7	16.43
Malignant histiocytoma				0.07
Reticulosarcoma		0.22		
Osteochondroma		0.04		
Chondroma		0.04		
Fibrochondroma		0.02		
Osteosarcoma				0.39
Osteochondrosarcoma		0.02		
Sarcoma	2.5	0.09		
Large cell sarcoma	1.25		0.5	
Round cell sarcoma	2.5			
Polymorph cell sarcoma	2.75			
Spindle cell sarcoma	3			
Unclassified tumors		0.62		
Ceruminal gland hyperplasia		0.13	0.1	
(Ceruminal cyst/hyperplasia)***				
Sebaceous gland hyperplasia		5.99	2.5	
Meibomian gland hyperplasia			0.1	
Hepatoid gland hyperplasia		0.82		
Epidermoid cyst			2.3	3.85
Dermoid cyst				0.15
Follicle cyst		7.06	1.4	0.91
Apocrine cyste			0.9	0.49
Sweat gland hyperplasia		0.09		
Cutanous fibrous polyp		5.72		
Collagenous naevus				1.76
Adnexal naevus (Organoid naevus)****			2.7	5.12
Skin tag			1	
Calcinosis cutis		1.18		
Keloid		0.09		
Other cysts		1.26		
Others			0.5	

*Frese (1960), ** Eskens (1983), *** Goldschmidt and Shofer (1992), **** Bomhard (2001)

Tab. 42: Sex distribution in dogs by different authors

Dog/ Litrature	*Frese, 1960, n=346*				*Goldschmidt, 1992*				*Bomhard, 2001*			
Tumor/ Sex	♂		♀		♂		♀		♂		♀	
	%	n	%	n	%	n	%	n	%	n	%	n
Basal cell tumor	71	5	29	2	46.5	510	53.5	586	56.93	1510	43.07	1142
Basal cell carcinoma									61.00	3	39.00	2
Basosquamous carcinoma					40.8	55	59.2	79				
Papilloma	67	6	33	3	42.9	18	57.1	24	50.32	316	49.68	312
Squamous cell carcinoma	61	17	39	11	43.9	116	56.1	148	55.02	735	44.98	600
Sebaceous adenoma (and hyperplasia)****	71	12	29	5	46	547	54	642	60.51	1987	39.49	1297
Sebaceous carcinoma					50.5	105	49.5	103	58.00	29	42.00	21
Hepatoid gland adenoma	89	58	11	7	76	2052	24	648	88.92	2385	11.08	297
Hepatoid gland carcinoma					90.3	131	9.7	14				
Meibomian gland adenoma					44	385	56	491				
Apocrine adenoma , (Syringoma)*, (papillary-)**, (Hidradenoma)****	100	1	0	0	45.1	208	54.9	253	59.78	368	40.22	248
Apocrine ductal adenoma					44.4	63	55.6	79				
Fibrocystadenoma	100	1	0	0								
Fibroadenoma papilliform	50	1	50	1								
Adenoma	100	4	0	0								
Apocrine carcinoma (papillary)**					40.9	88	59.1	127	51.85	14	48.15	13
Carcinoma	90	9	10	1								
Adenocarcinoma	67	6	33	3								
Ceruminal gland adenoma					53.8	45	46.2	38	75.01	10	24.99	3
Ceruminal gland carcinoma									53.49	22	46.51	19
Anal sac gland carcinoma					43.7	104	56.3	134	26.54	56	73.46	154
Trichoepithelioma					34.1	407	65.9	788	52.07	604	47.93	556
Epithelioma Malherbe	100	2	0	0	47.1	124	52.9	139	45.09	802	54.91	977
Intra-cutaneous cornifying epithelioma	67	4	33	2	47.1	248	52.9	279	53.20	541	46.80	476
Benigne melanoma	57	12	43	9	49.5	482	50.5	491	60.84	1125	39.16	724
Malignant melanoma, (Canine cutanous)***	59	10	41	7	49.7	71	50.3	72	61.41	540	38.59	339
Malignant melanoma, (Canine subungual)***					44.8	43	55.2	53				
Malignant melanoma, (Lip)***					53.6	161	46.4	139				
Fibroma	36	5	64	9	47.7	295	52.3	323	51.21	423	48.79	403
Myxoma	100	1	0	0	22.2	2	77.8	7				
Myxosarcoma					40.6	71	59.4	104				
Hemangiopericytoma					34	659	66	1280				

Continue tab. 42

Dog/ Litrature	*Frese, 1960*				*Goldschmidt, 1992*				*Bomhard, 2001*			
Tumor/ Sex	♂		♀		♂		♀		♂		♀	
	%	n	%	n	%	n	%	n	%	n	%	n
Fibrosarcoma	75	9	25	3	40.9	185	59.1	267	48.84	1725	51.16	1807
Lipoma	63	5	38	3	31.7	638	68.3	1375	31.14	876	68.86	1936
Infiltrative lipoma					35.1	78	64.9	144				
Liposarcoma	0	0	100	1	51.9	41	48.1	38	70.22	67	29.78	28
Hemangioma	38	5	62	8	43	559	57	742	49.03	686	50.97	713
Perithelioma	0	0	100	1	45.7	132	54.3	157				
Lymphangioma	100	1	0	0	39.1	9	60.9	14				
Hemangiosarcoma (Angiosarcoma)*	0	0	100	1					65.10	373	34.90	200
Leiomyoma (Myoma)*	100	1	0	0					23.08	15	76.92	49
Leiomyosarcoma									25.00	1	75.00	3
Neurofibroma									48.89	22	51.11	24
Neurofibrosarcoma									37.50	4	62.50	6
Benign peripheral nerve sheath tumor					51.9	14	48.1	13				
Malignant peripheral nerve sheath tumor					44.3	43	55.7	54				
Mast cell tumor	68	17	32	8	39.4	982	60.6	1510	48.51	1753	51.49	1861
Malignant lymphoma	100	1	0	0	44.6	116	55.4	144	55.51	131	44.49	105
Mycosis fungoides									56.25	56	43.75	44
Extramedullary plasmocytoma					48.3	215	51.7	230	59.25	363	40.75	250
Histicytoma (benign round cell sarcoma)*	69	18	31	8	52	1818	48	1679	59.23	4382	40.77	3017
Malignant histiocytoma (Giant cell tumor of soft tissue)***					33.4	3	66.6	6	58.06	19	41.94	14
Osteosarcoma									47.71	84	52.29	92
Sarcoma	88	7	13	1								
Large cell sarcoma	40	2	60	3								
Round cell sarcoma	70	7	30	3								
Polymorph cell sarcoma	50	5	50	5								
Spindle cell sarcoma	67	6	33	3								
Sebaceous gland hyperplasia					41.3	290	58.7	413				
Epidermoid cyst					41.7	272	58.3	380	50.29	874	49.71	864
Dermoid cyst									55.22	38	44.78	31
Follicle cyst					45.4	179	54.6	215	41.85	172	58.15	239
Apocrine cyste					45	109	55	133	56.00	125	44.00	98
Collagenous naevus									45.62	365	54.38	435
Adnexal naevus (Organoid naevus)****					45.4	359	54.6	431	58.58	1354	41.42	957
Skin tag					45.2	133	54.8	161				
Total	**69**	**238**	**31**	**108**		**13165**		**15147**		**24955**		**20357**

*Frese (1960), ** Eskens (1983), *** Goldschmidt and Shofer (1992), **** Bomhard (2001)

Tab. 43: Tumor distribution in cats by two authors

Tumor	Goldschmidt and Shofer (1992) %	Bomhard (2001) %
Basal cell tumor	14.2	15.39
Basal cell carcinoma	1.3	0.52
Papilloma		0.15
Basosquamous carcinoma	0.4	
Squamous cell carcinoma	9.6	6.18
Sebaceous adenoma	1.7	0.94
Sebaceous carcinoma	0.8	0.06
Meibomian gland adenoma	0.4	
Apocrine cyst	1.2	0.47
Apocrine adenoma (Hidradenoma)*	2.9	5.63
Apocrine ductal adenoma	2.1	
Apocrine carcinoma	2.5	0.09
Ceruminous gland adenoma	2.5	0.14
Ceruminous gland carcinoma	2.9	2.19
Anal sac gland carcinoma	0.4	0.10
Trichoepithelioma	0.8	0.10
Epithelioma Malherbe	0.4	0.05
Intracutaneous cornifying epithelioma		0.10
Epidermoid cyst	3.7	2.54
Dermoid cyst		0.07
Follicle cyst	0.8	0.05
Benign melanoma	0.6	0.38
Malignant melanoma	0.4	1.33

Tumor	Goldschmidt and Shofer (1992) %	Bomhard (2001) %
Fibroma		1.25
Fibrosarcoma	16.6	43.89
Myxomatous tumors	0.9	
Lipoma	5.5	4.17
Liposarcoma	0.5	0.10
Hemangioma	1.8	1.03
Hemangiosarcoma	2.8	1.95
Lymphangioma	0.5	
Leiomyosarcoma		0.01
Neurofibroma		0.81
Neurofibrosarcoma		0.15
Neural tumors (not further specified)	1.4	
Mast cell tumor	12.4	5.52
Malignant lymphoma	2.8	2.58
Mycosis fungoides		0.18
Extramedullary plasmocytoma	0.5	0.20
Malignant histiocytoma		0.21
Giant cell tumor of soft tissue	0.9	
Osteosarcoma		1.03
Adnexal naevus (Organoid naevus*)	0.1	0.24
Collagenous naevus		0.21
Ceruminous cyst/ hyperplasia	1.8	
Sebaceous hyperplasia	1	

*Bomhard (2001)

Tab. 44: Skin cysts

Cysts	*Origin*	*Location*	*Lined by*	*Outer wall& Tissue*	*Contents*	*Others*
Infundibular cyst	Epidermis or infundibulum[1] (can also develop after traumatic implantation of the epidermis into the dermis)[2,4]	Within the dermis, but large cysts may extend into the panniculus adiposus. A small pore may be found between the cyst and the overlying epidermis	Stratified squamous epithelium, all four layers including the granular cell layer (The epithelial wall may become very thin)[4]	The basal layer of the cyst wall abuts dermal collagen in a smooth line[4]	The cornified cells that occupy the cyst are loosely packed (basketweave orthokeratosis) or tightly compressed(compact orthokeratosis)1 Some cysts may contain fragments of mature hair shafts.[4]	Persistent cysts may develop into squamous carcinomas.[4] Rupture of the cyst wall will evoke a granulomatous inflammation
Dilated pore (of Winer)[4]	Dilated infundibulum	The cyst communicates with the overlying epidermis via a **pore that may be quite wide[1], (on the head or neck)**	Like infundibular cyst, but with **hyperplastic epithelium** forming the deeper portions of the cyst wall	Outer wall consists of hyperplastic epithelium **with characteristic rete ridges[1] (in parallel columns)**[4]	Compact laminated keratin that can protrude through the pore, forming a **cutaneous horn**	**Middle-aged or old cats**[4]
Isthmus cyst	Middle segment of the anagen follicle and lower segment of the catagen follicle	Not mentioned	Stratified squamous keratinizing epithelium, but **lacks a granular cell layer**. The keratinocytes above the basal layer have abundant pale eosinophilic cytoplasm, and intercellular bridges are difficult to identify	Not mentioned	Less eosinophilic and less compact or laminar than those of an infundibular cyst	
Panfollicular cyst	Follicular epithelium	Not mentioned	Lined by stratified epithelium with foci of changes as described above for the Infundibular and Isthmus cysts. **A third type of cell lining the cyst wall consists of primitive, small basophilic cells that schow abrupt keratinization**. Small foci of cells with intracytoplasmic trichohyalin granules may be found between zones of infundibular and matrical keratinization	Not mentioned	**Shadow cells**	These cysts may progress to trichoepitheliomas
Dermoid cyst	Congenital	Often found on the midline (of the back)[3], dermal or subcutaneous, may communicate with the overlying epidermis via a small pore	Epidermis (stratified squamous keratinizing epithelium) with mature (or primitive)[4] dermal and adnexal structures (**hair follicles and sebaceous glands**) (sweat gland differentiation theoretically possible but rarely seen)[4]	**Rete pegs are present**[3]	**Hair and keratin**[1] (usually less keratinization than in epidermoid cyst)[4]	In the young animals (noted soon after birth)[2]. Dermoid cyst of Rhodesian ridgeback dogs occurring along the dorsal midline[4]
Sebaceous duct cyst	Sebaceous duct	Intradermal	Squamous epithelium consists of basaloid cells and squamous cells. The inner lining of the cyst is Brightly eosinophilic and corrugated. A granular Cell layer is often difficult to identify.	**Surrounded by. hyperplastic sebaceous glands**	Not mentioned	
Apocrine cyst	Apocrine secretory epithelium	Intradermal	Single layer of apocrine secretory epithelium, the cells often become flattened due to pressure atrophy	Not mentioned	Fluid	Multiple cysts at multiple sites are referred to as apocrine cystomatosis
Ciliated cyst	Probably represent a developmental defect[2]	Found in the **neck, intradermal**[2]	**Cuboidal to columnar epithelial cells, most of which have cilia**. Occasional goblet cells are interspersed between the ciliated cells	Not mentioned	Fluid[2]	**Only in cats**[2]
Subungual epithelial inclusion cyst	Subungual epithelialium	Present within the **bone of the third phalanx**	Identical to the infundibular cyst.	**Surrounded by the bone** of the third phalanx	Keratin	Rupture of the cyst wall will evoke a granulomatous inflammation
Pressure point comedones	Follicular infundibular epithelium	Occur primarily at the **elbow**	Stratified squarnous epithelium with prominent granular cell layer. Remnants of hair follicles and sebaceous glands may be found in the wall of the cyst	Not mentioned	Hair and loose keratin	Simple cysts and may be multiple. Rupture of the cyst wall will evoke a granulomatous inflammation

1- Goldschmidt et al. (1998), 2- Goldschmidt and Shofer (1992), 3- Weiss and Frese (1974), 4- Jubb et al. (1993).

8.2. Abbreviations

ABC	Avidin-Biotin-Complex
BSA	Bovine serum albumin
DAB	Diaminobenzidin-tetrahydrochlorid
Diag.	Diagram
e.g.	As example
ESH cat	European shorthair cat
Fig.	Figure
GFAP	Glial fibrillary acidic protein
i.e.	id est = that is
Ig	Immunglobulin
M	Molar
min	Minute
MPNST	Malignant peripheral nerve sheath tumor
n	Number
NSE	Neuron Specific Enolase
PBS	Phosphate-buffered saline
rpm	Round per minute
sec.	Second
SS	Swine serum
Tab.	Table
TBS	Tris-buffered saline
TNM	The extent of the primary tumor (T), the condition of the regional lymph nodes (N), and the presence or absence of distant metastasis (M) (Matyas, 1982)
USA	United States of America
WHO	World Health Organisation

8.3. Figures

8.3.1. Follicular tumors

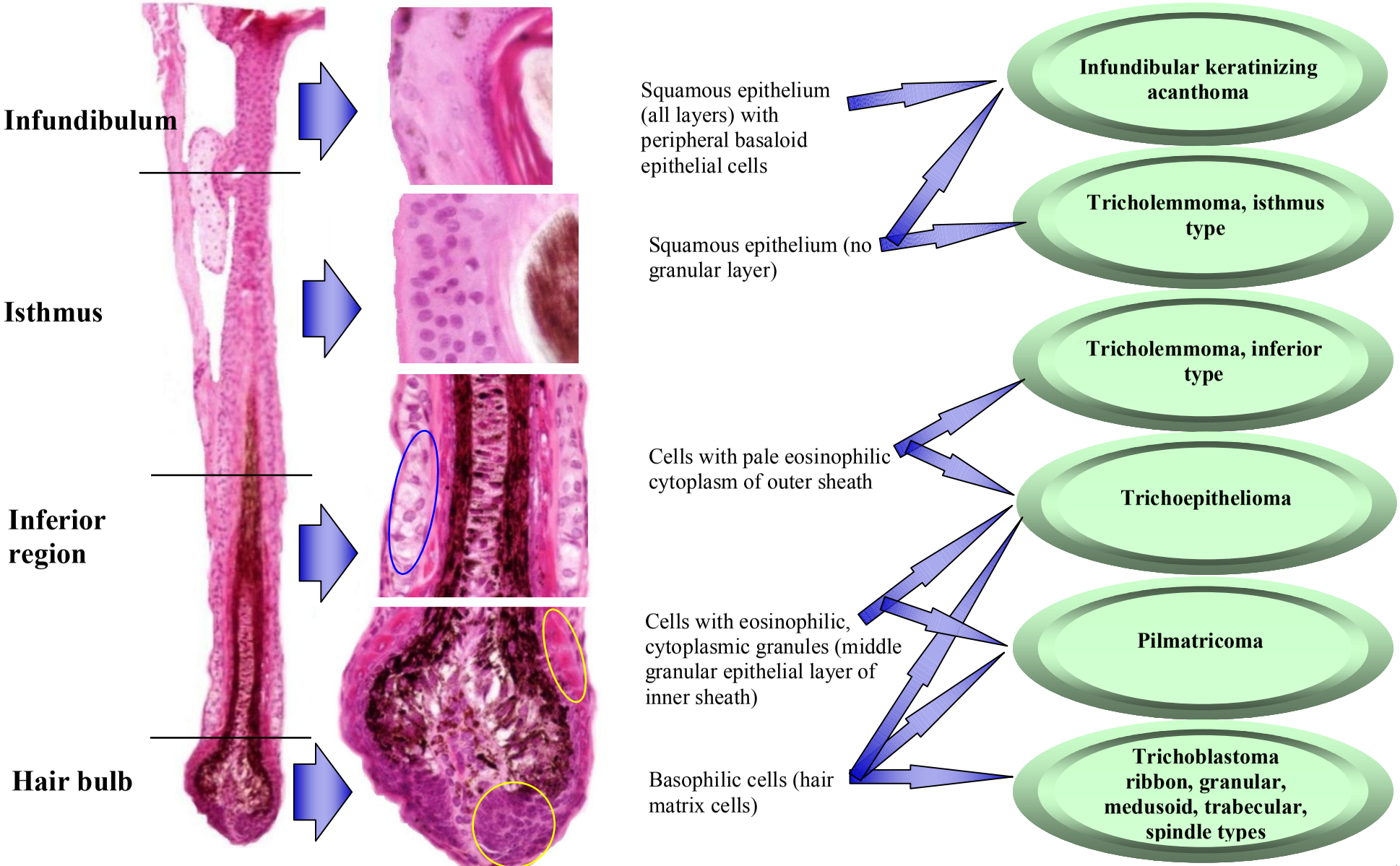

Fig. 1a: Hair follicle and its tumors. HE. (Obj.: 10 & 40X).

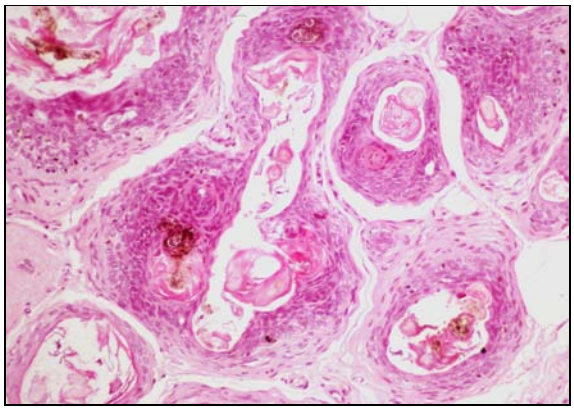

Fig. 1b: T732/00. Trichoepithelioma, note the abortive trichogenic differentiation and abrupt and gradual keratinization. HE. (Obj.: 20X), dog

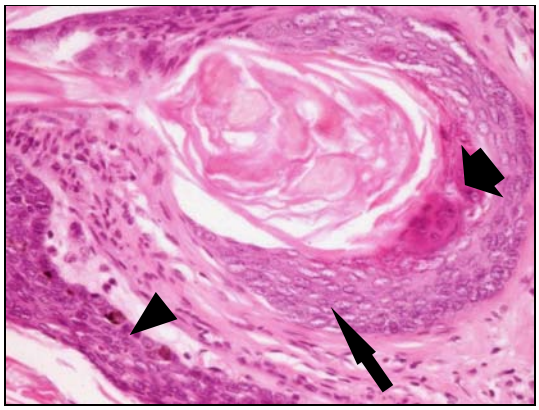

Fig. 1c: T732/00. Trichoepithelioma, with different cell population, basaloid (arrow head), granular (thick arrow) and tricholemmal differentiation (thin arrow). HE. (Obj.: 40X), dog

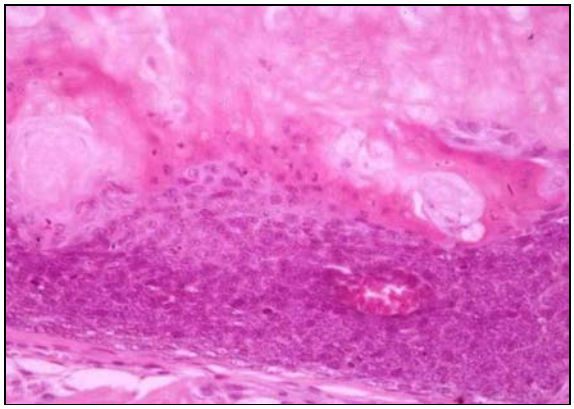

Fig. 1d: T3384/00. Pilomatricoma, note the abrupt keratinization, the eosinophilic cytoplasm and the remnants of the cells nuclei. HE. (Obj.: 40X), dog

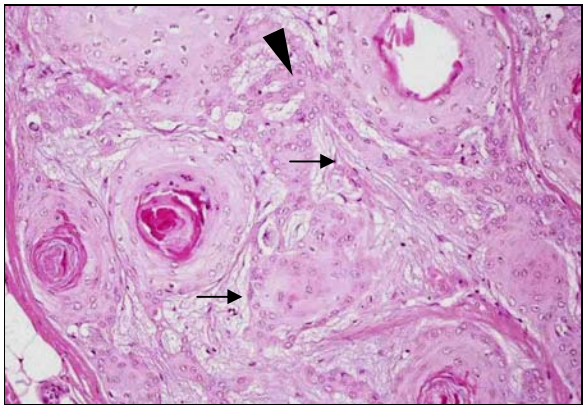

Fig. 1e: T316/00. Infundibular keratinizing acanthoma, note the cords of epithelial cells (arrow head) and the stromal mucinosis (arrows). HE. (Obj.: 20X), dog

8.3.2. Basal cell tumor and trichoblastoma

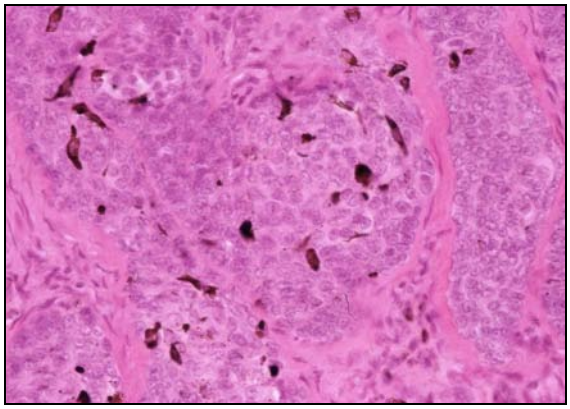

Fig. 2a: T1120/00. Basal cell tumor, solid type. HE. (Obj.: 40X), cat

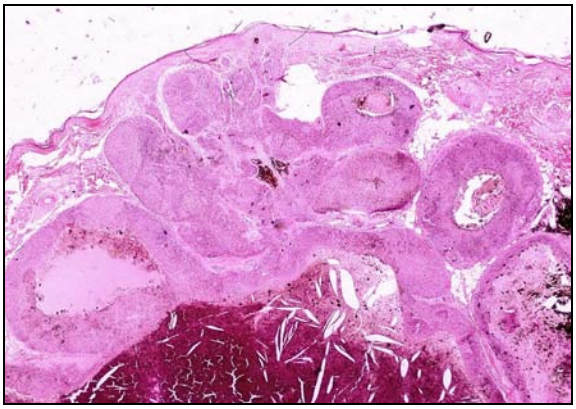

Fig. 2b: T1439/00. Basal cell tumor, cystic variant. HE. (Obj.: 2.5X), cat

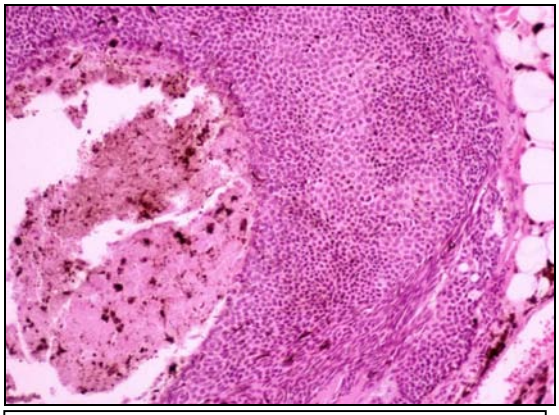

Fig. 2c: T1439/00. Basal cell tumor, cystic variant. HE. (Obj.: 20X), cat

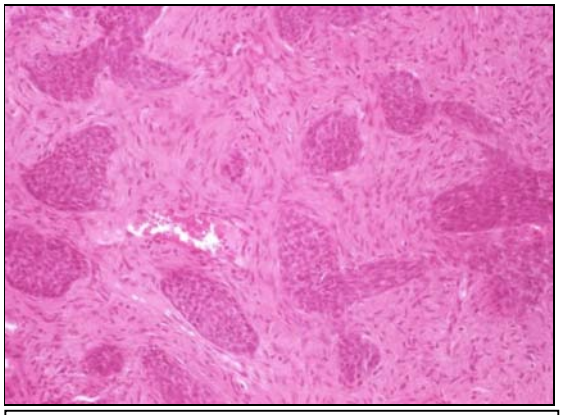

Fig. 2d: T1196/05. Infiltrative basal cell carcinoma. HE. (Obj.: 20X), cat

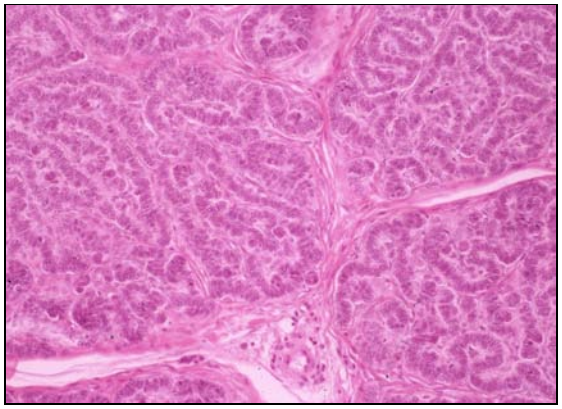

Fig. 2e: T2402/00. Trichoblastoma, ribbon type. HE. (Obj.: 20X), dog

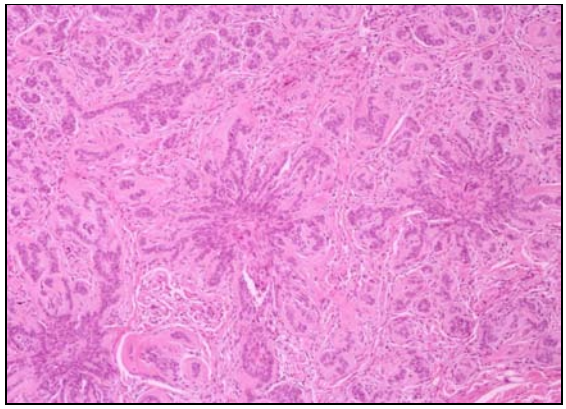

Fig. 2f: T1955/00. Trichoblastoma, medusoid type. HE. (Obj.: 10X), dog

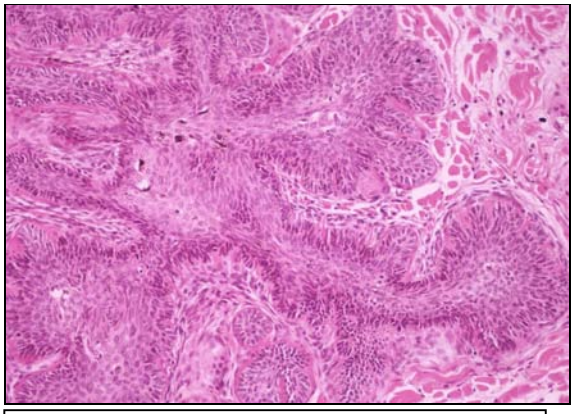

Fig. 2g: T2183/00. Trichoblastoma, trabicular type. HE. (Obj.: 20X), cat

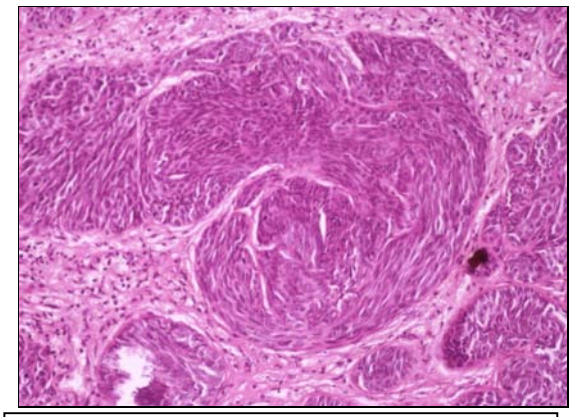

Fig. 2h: T171/00. Trichoblastoma, spindle cell type. HE. (Obj.: 20X), cat

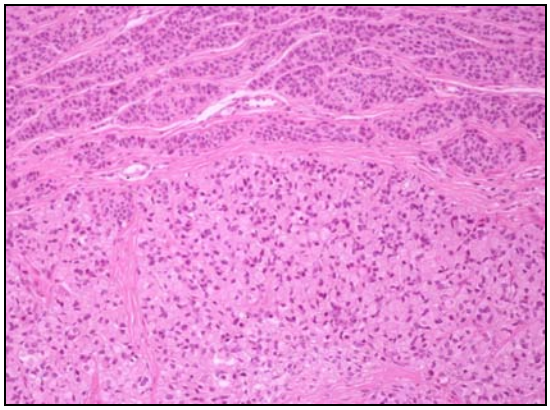

Fig. 2i: T681/00. Trichoblastoma, granular cell type. HE. (Obj.: 20X), dog

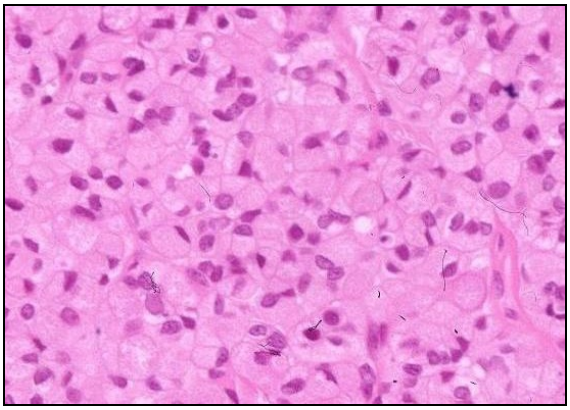

Fig. 2j: T681/00. Trichoblastoma, granular cell type. HE. (Obj.: 40X), dog

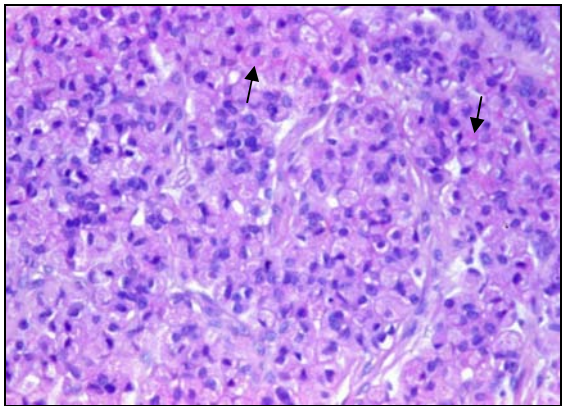

Fig. 2k: T681/00. Trichoblastoma, granular cell type with PAS positive cytoplasmic granules (arrows). PAS. (Obj.: 40X), dog

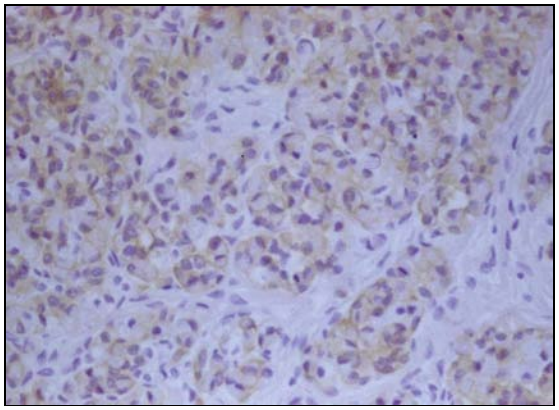

Fig. 2l: T681/00. Trichoblastoma, granular cell type. Immunoperoxidase, Cytokeratin. (Obj.: 40X), dog

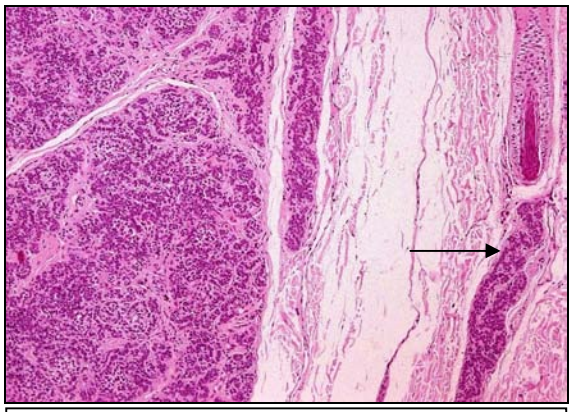

Fig. 2m: T2991/00. Trichoblastoma, clear cell variant, tumor mass with ribbon like pattern. Note the growing of the neoplastic cells at the base of a hair follicle (arrow). HE. (Obj.: 10X), dog

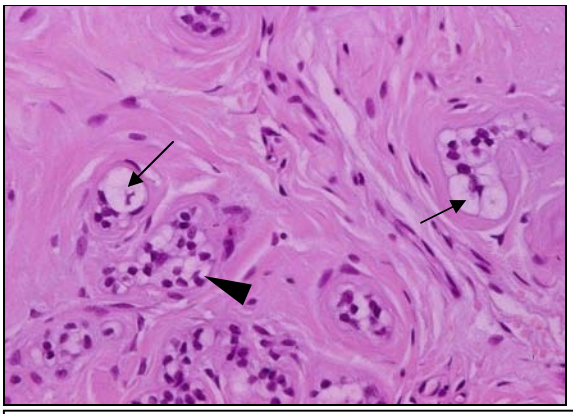

Fig. 2n: T2991/00. Trichoblastoma, clear cell variant, neoplastic cells in small nests with many large vacuolated cells (sebocytes) (arrows) and other cells with pale cytoplasm (arrow head). HE. (Obj.: 40X), dog

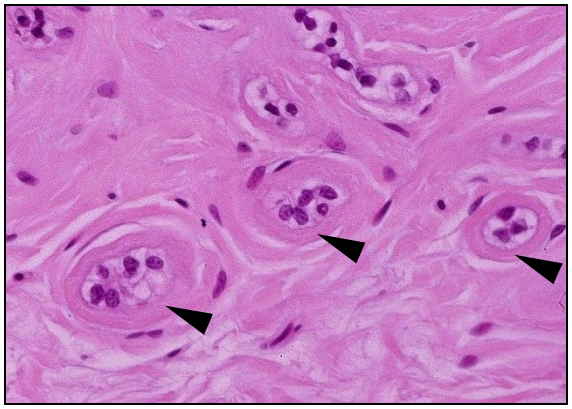

Fig. 2o: T2991/00. Trichoblastoma, clear cell variant, neoplastic cells in small islands have pale cytoplasm surrounded by sclerotic basal membrane (arrow heads). HE. (Obj.: 40X), dog

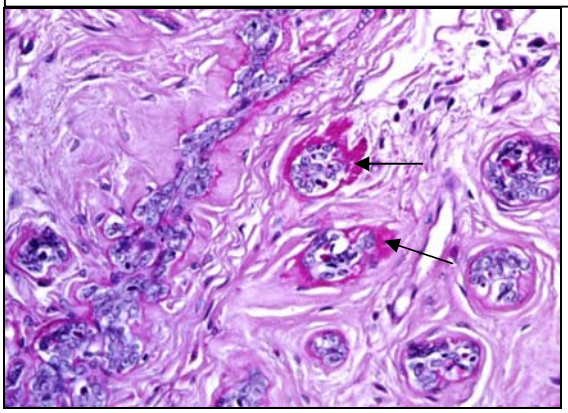

Fig. 2p: T1310/00. Trichoblastoma, clear cell variant, neoplastic cells in small islands surrounded by PAS-positive sclerotic basal membrane. PAS (arrows). (Obj.: 40X), dog

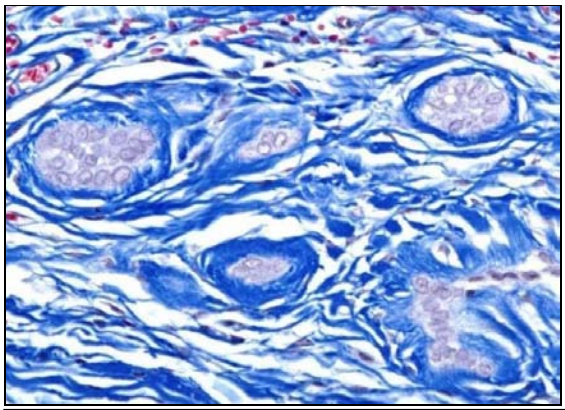

Fig. 2q: T2991/00. Trichoblastoma, clear cell variant, neoplastic cells in small islands surrounded by peripheral, blue, sclerotic basal membrane. Masson's trichrome stain. (Obj.: 40X), dog

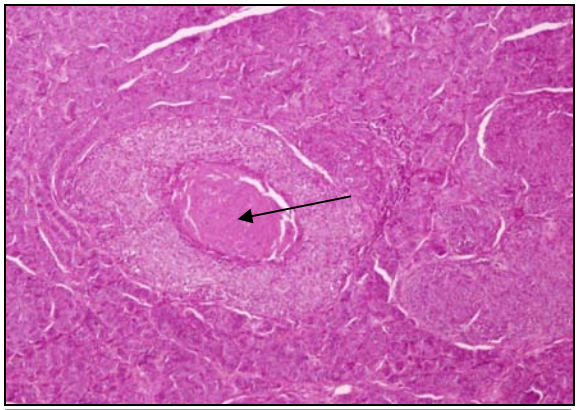

Fig. 2r: T1462/00. Trichoblastoma, ribbon type with necrosis (arrow) (cystic type). HE. (Obj.: 10X), cat

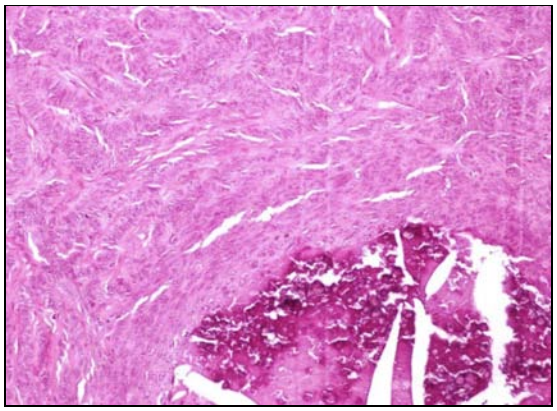

Fig. 2s: T1462/00. Trichoblastoma, ribbon type with necrosis and calcification (cystic type). HE. (Obj.: 20X), cat

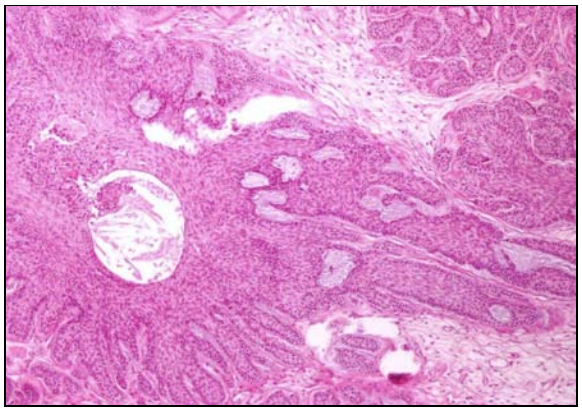

Fig. 2t: T1166/00. Trichoblastoma, trabecular type with mucoid degeneration (cystic type). HE. (Obj.: 10X), cat

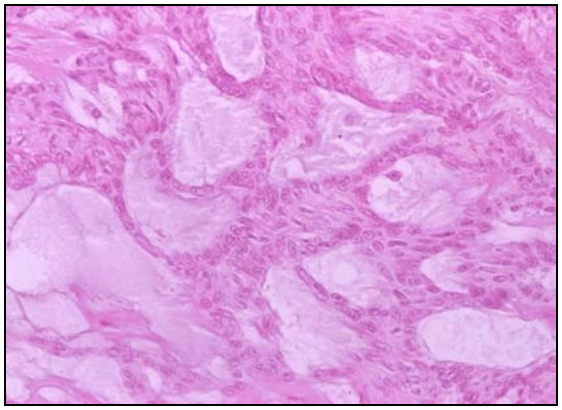

Fig. 2u: T1166/00. Trichoblastoma, trabecular type with mucoid degeneration. HE. (Obj.: 40X), cat

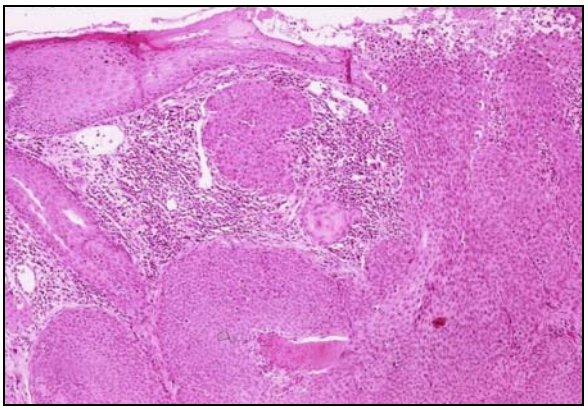

Fig. 2v: T3220/00. Basal cell tumor associated with the overlying epidermis. HE. (Obj.: 10X), dog

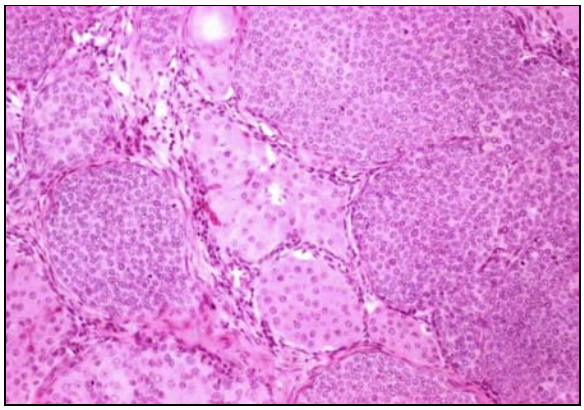

Fig. 2w: T3220/00. Basal cell tumor adjacent to hepatoid gland hyperplasia. HE. (Obj.: 20X), dog

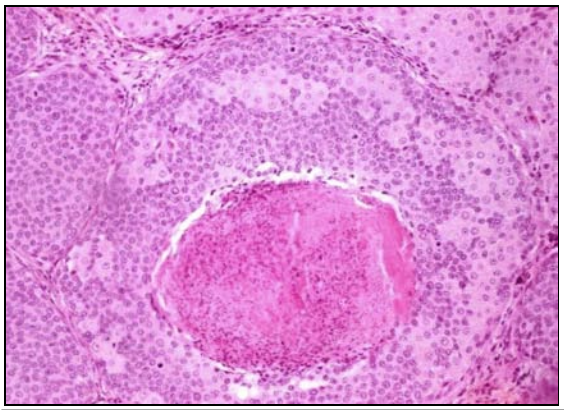

Fig. 2x: T3220/00. Basal cell tumor mixed with hepatoid cells and with hepatoid gland hyperplasia. HE. (Obj.: 20X), dog

8.3.3. Viral induced papilloma and squamous papilloma

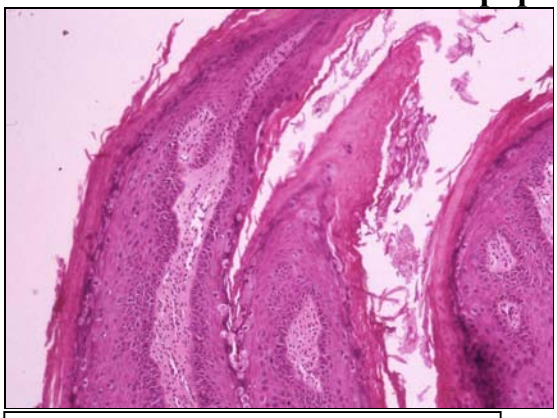

Fig. 3a: T1789/00. Papilloma. HE. (Obj.: 10X), dog.

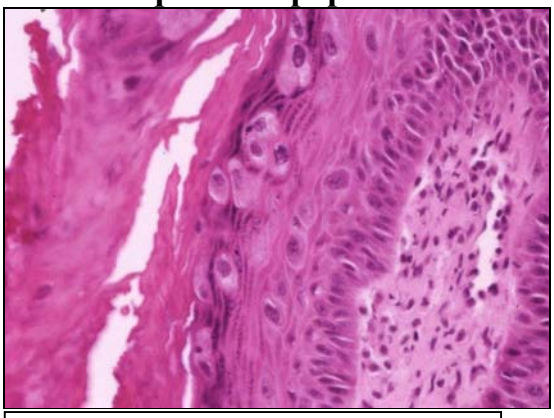

Fig. 3b: T1789/00. Papilloma. HE. (Obj.: X), dog.

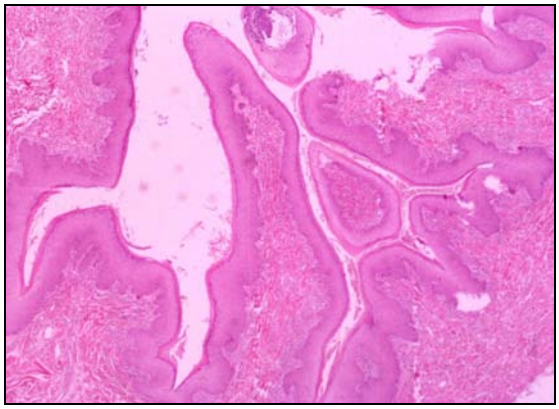

Fig. 3c: T2618/00. Squamous papilloma. HE. (Obj.: 2.5X), dog.

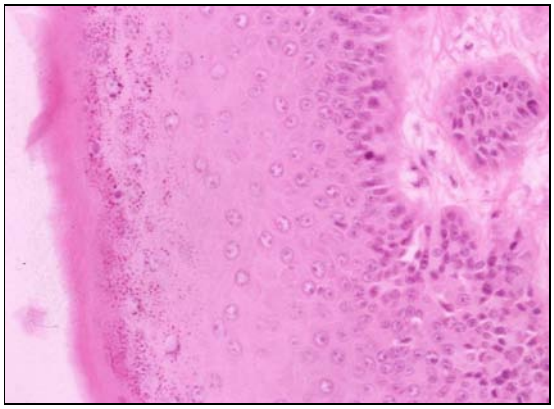

Fig. 3d: T2618/00. Squamous papilloma. HE. (Obj.: 40X), dog.

8.3.4. Nailbed tumors

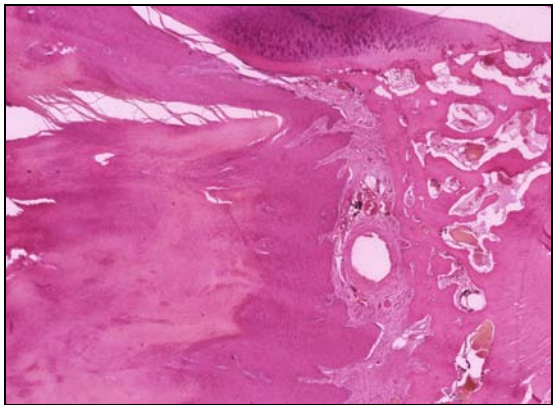

Fig. 4a: T840/00. Subungual keratoacanthoma. HE. (Obj.: 2.5X), dog.

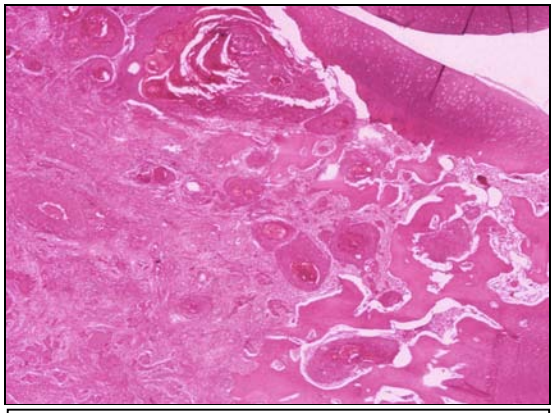

Fig. 4c: T2886/00. Subungual squamous cell carcinoma. HE. (Obj.: 2.5X), dog.

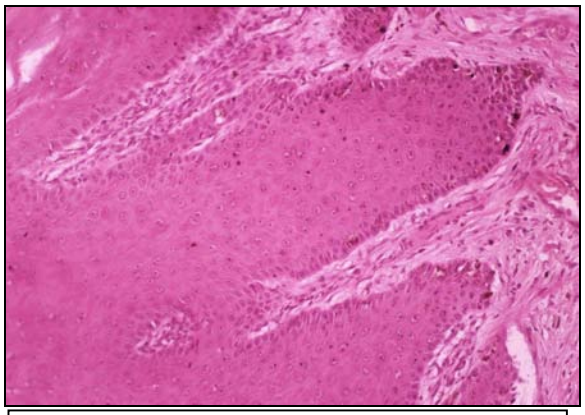

Fig. 4b: T840/00. Subungual keratoacanthoma. HE. (Obj.: 20X), dog.

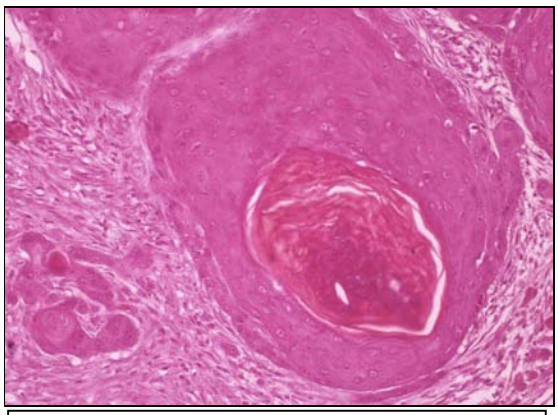

Fig. 4d: T2886/00. Subungual squamous cell carcinoma. HE. (Obj.: 20X), dog.

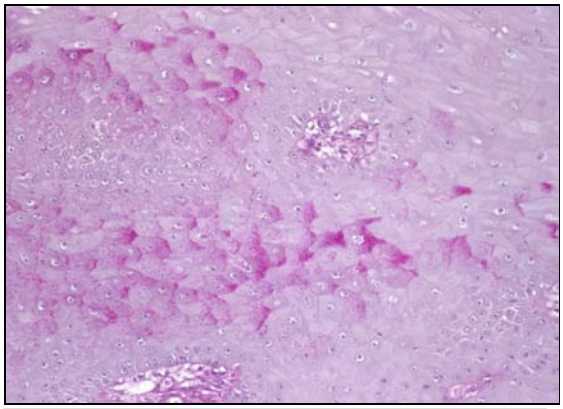

Fig. 4e: T840/00. Subungual keratoacanthoma. PAS. (Obj.: 20X), dog.

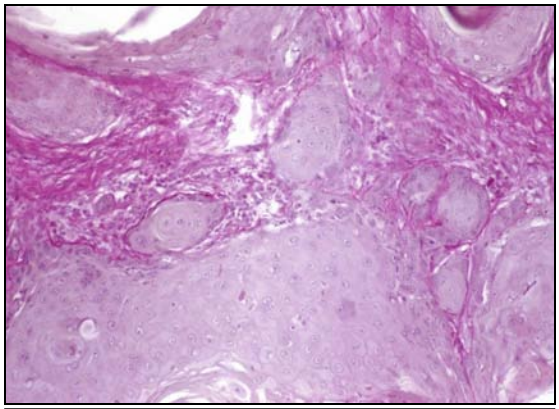

Fig. 4f: T2886/00. Subungual squamous cell carcinoma. PAS. (Obj.: 20X), dog.

8.3.5. Bowen-like disease and basosquamous carcinoma

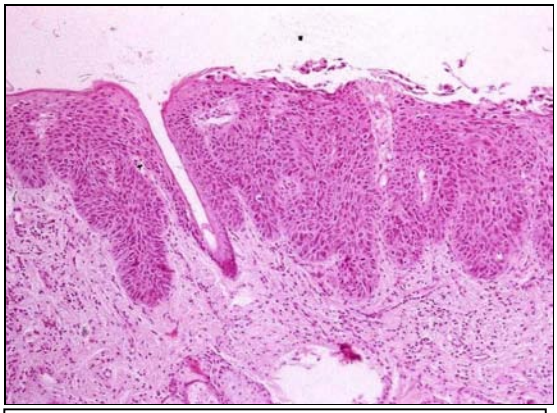

Fig. 5a: T1172/00. Bowen-like disease. HE. (Obj.: 10X), cat.

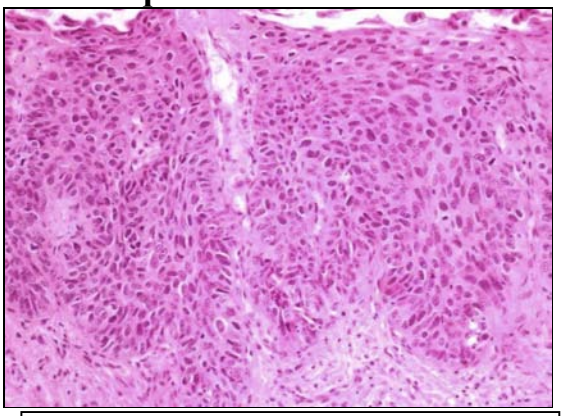

Fig. 5b: T1172/00. Bowen-like disease. HE. (Obj.: 20X), cat.

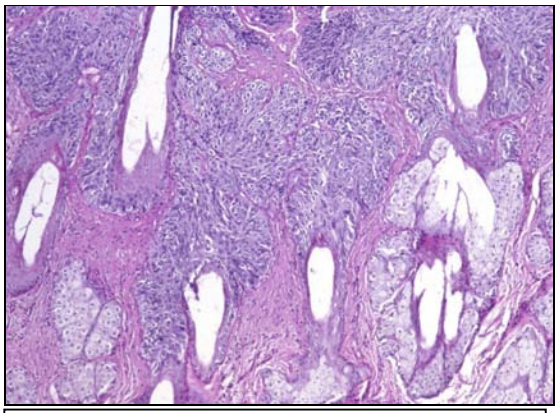

Fig. 5c: T1172/00. Bowen-like disease. PAS. (Obj.: 20X), cat.

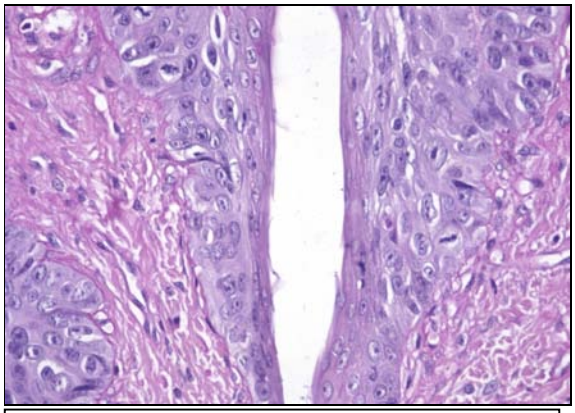

Fig. 5c: T1172/00. Bowen-like disease. PAS. (Obj.: 40X), cat.

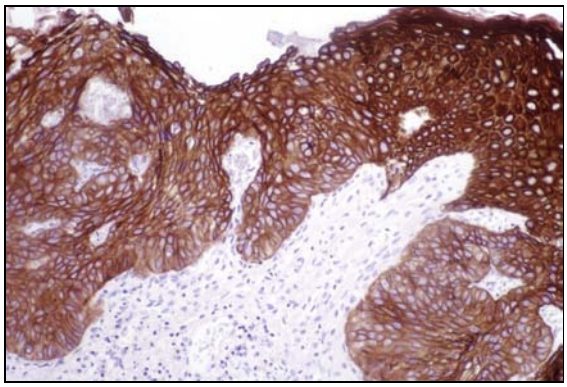

Fig. 5c: T1172/00. Bowen-like disease. Immunoperoxidase, Cytokeratin. (Obj.: 20X), cat.

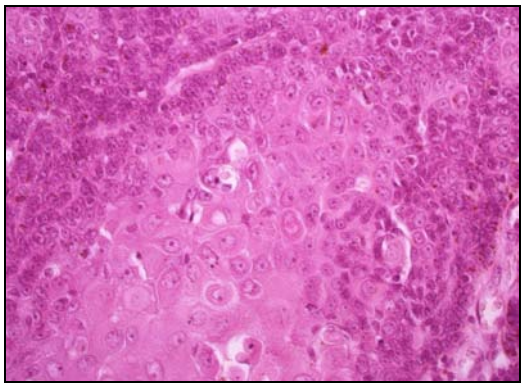

Fig. 5d: T885/00. Basosquamous carcinoma. HE. (Obj.: 40X), dog.

8.3.6. Skin cysts

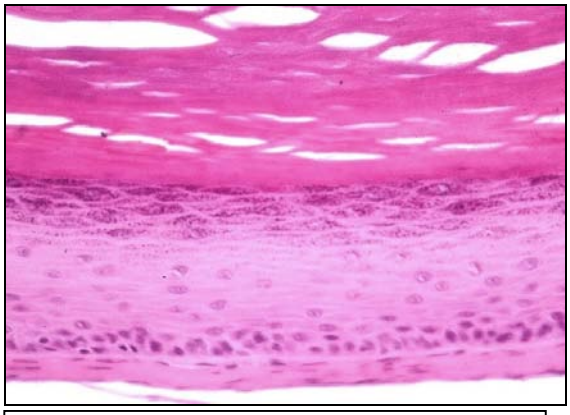

Fig. 6a: T1417/00. Infundibular cyst. HE. (Obj.: 40X), dog.

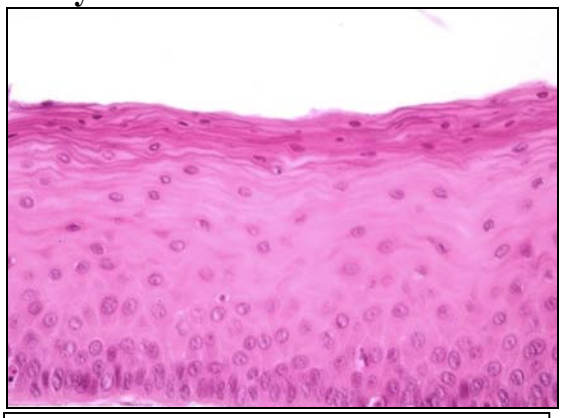

Fig. 6b: T824/00. Isthmus cyst, stratified squamous epithelium lacks a granular layer. HE. (Obj.: 40X), dog.

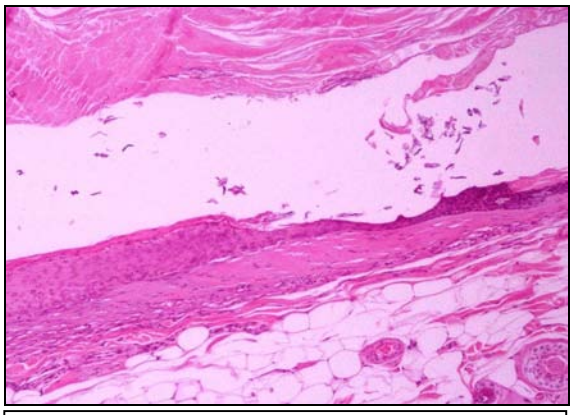

Fig. 6c: T1896/00. Panfollicular cyst. HE. (Obj.: 10X), dog.

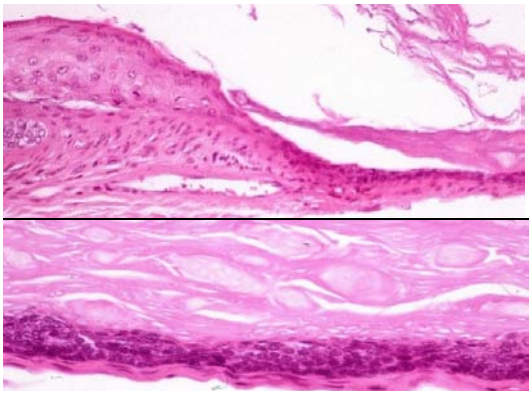

Fig. 6d: T1896/00. Panfollicular cyst, squamous epithelium transition to basaloid cell (above), basaloid cells with abrupt kerantization (below). HE. (Obj.: 40X), dog.

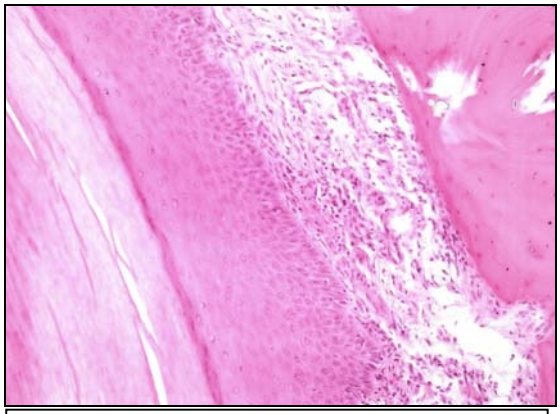

Fig. 6e: T1119/00. Subungual epithelial inclusion cyst. HE. (Obj.: 20X), dog.

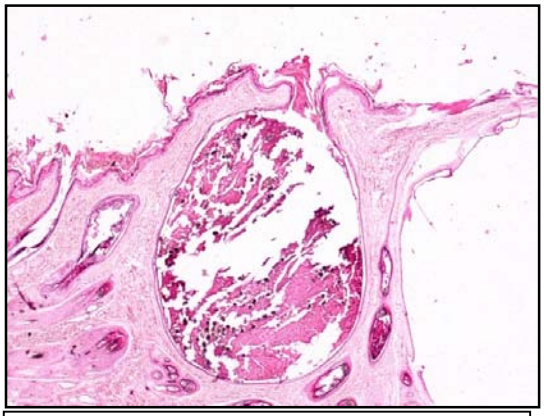

Fig. 6f: T1236/00. Pressure point comedones. HE. (Obj.: 2.5X), dog.

8.3.7. Hamartomas and tumorlike lesions

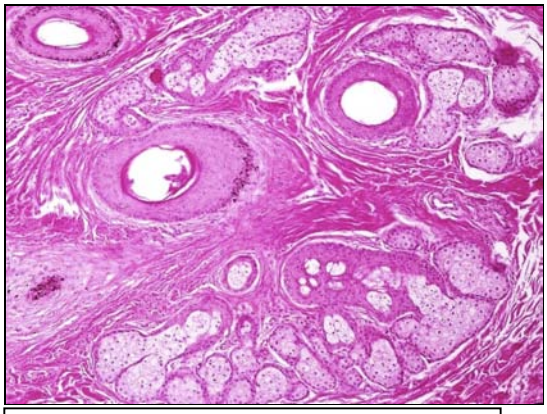

Fig. 7a: T1612/00. Fibroadnexal hamartoma. HE. (Obj.: 10X), dog.

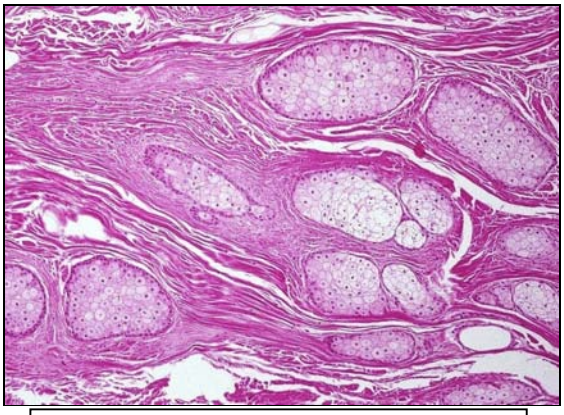

Fig. 7b: T3352/00. Sebaceous hamartoma. HE. (Obj.: 10X), dog.

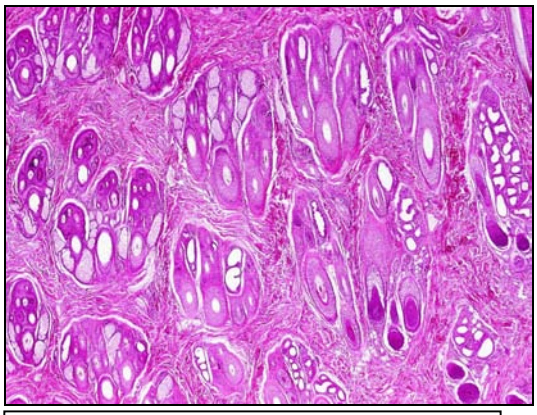

Fig. 7c: T1386/00. Follicular hamartoma. HE. (Obj.: 2.5X), dog.

8.3.8. Sebaceous and modified sebaceous gland tumors

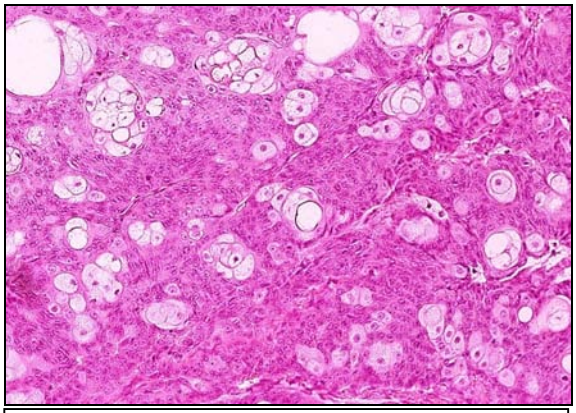

Fig. 8a: T1220/00. Sebaceous epithelioma. HE. (Obj.: 20X), dog.

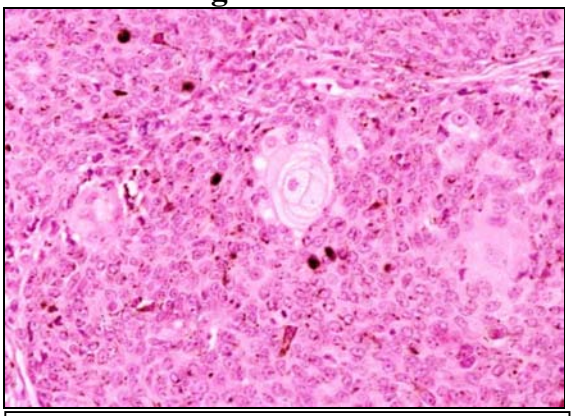

Fig. 8b: T1220/00. Sebaceous epithelioma. HE. (Obj.: 20X), dog.

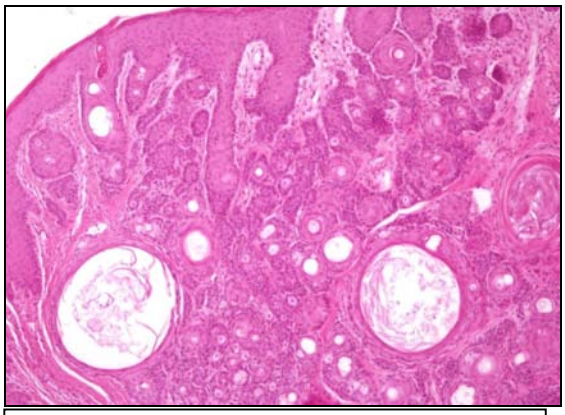

Fig. 8c: T4/04. Sebaceous ductal adenoma. HE. (Obj.: 10X), dog.

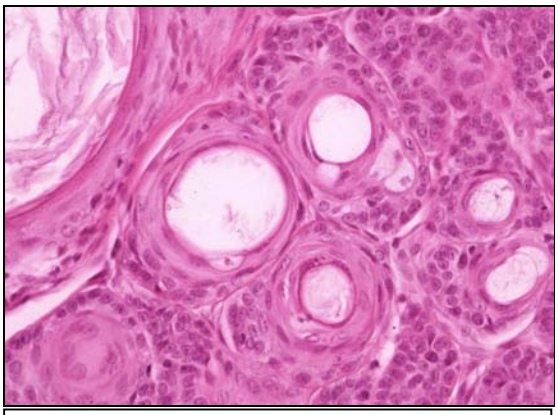

Fig. 8d: T4/04. Sebaceous ductal adenoma. HE. (Obj.: 40X), dog.

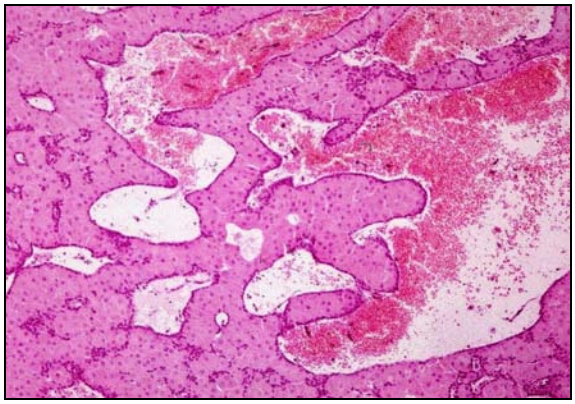

Fig. 8e: T3234/00. Hepatoid gland (angio-) adenoma. HE. (Obj.: 20X), dog.

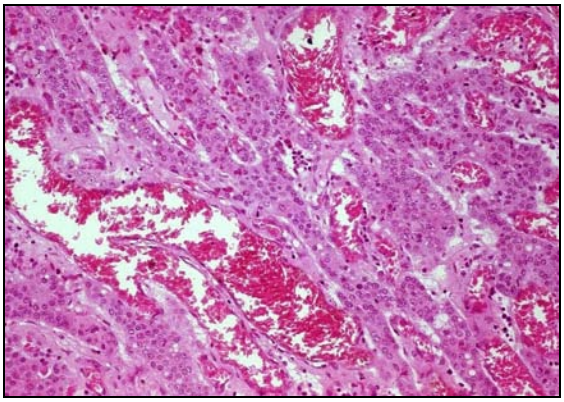

Fig. 8f: T442/00.Hepatoid gland (angio-) epithelioma. HE. (Obj.: 20X), dog

8.3.9. Fibroma and collagenous hamartoma

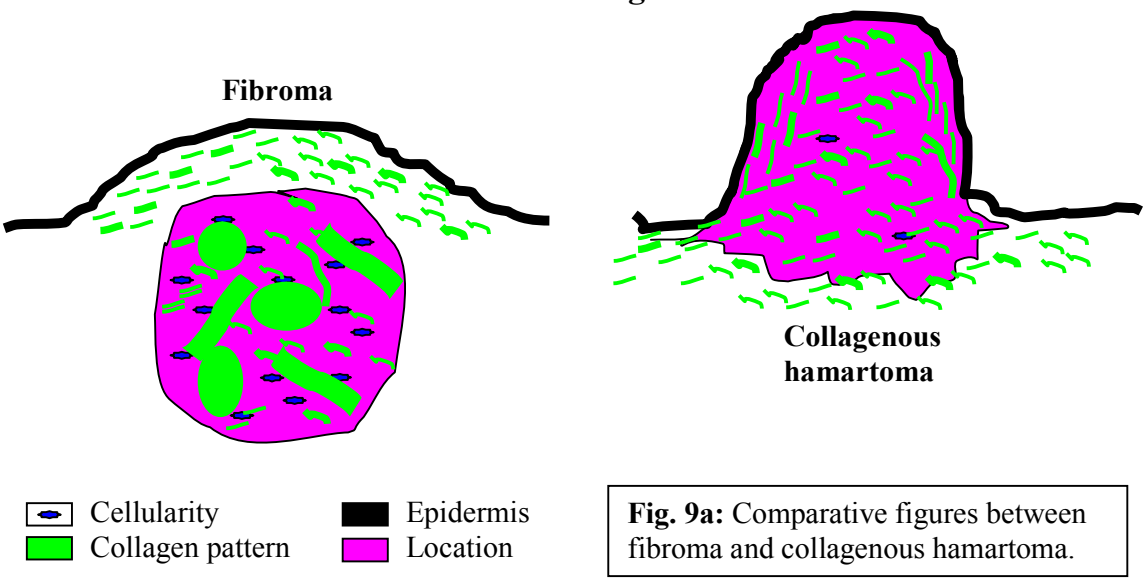

Fig. 9a: Comparative figures between fibroma and collagenous hamartoma.

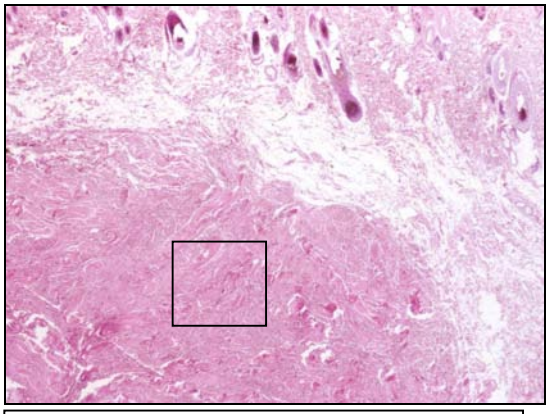

Fig. 9b: T140/00. Fibroma. HE. (Obj.: 2.5X), dog.

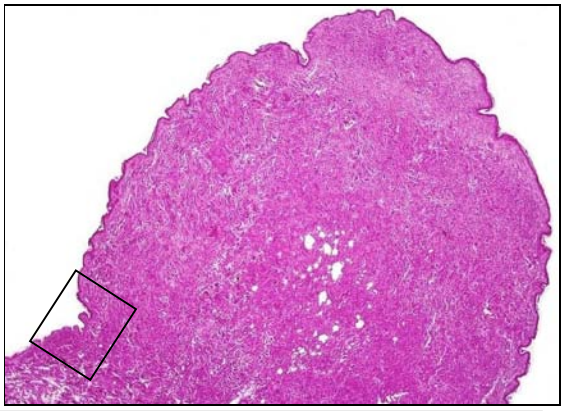

Fig. 9d: T1253/00. Collagenous hamartoma. HE. (Obj.: 1.25X), dog.

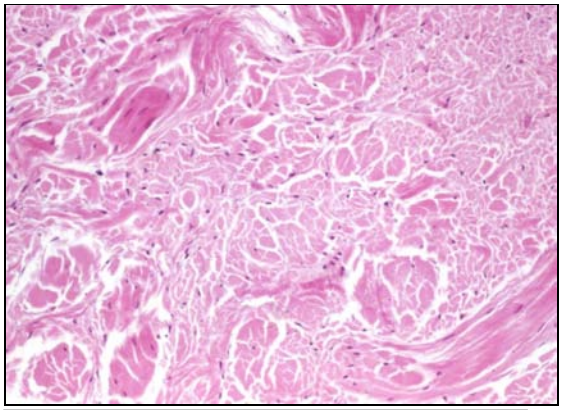

Fig. 9c: T140/00. Fibroma. HE. (Obj.: 20X), dog.

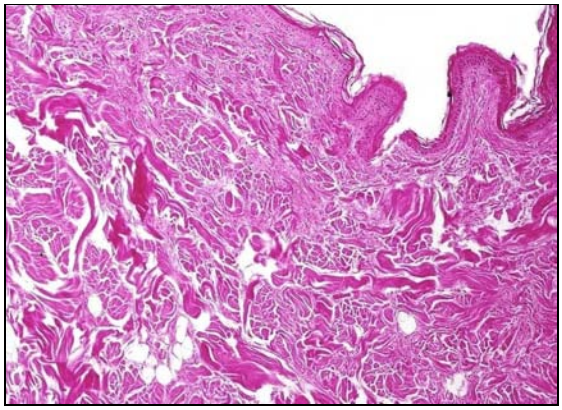

Fig. 9e: T1253/00. Collagenous hamartoma. HE. (Obj.: 10X), dog.

8.3.10. Peripheral nerve sheath tumors

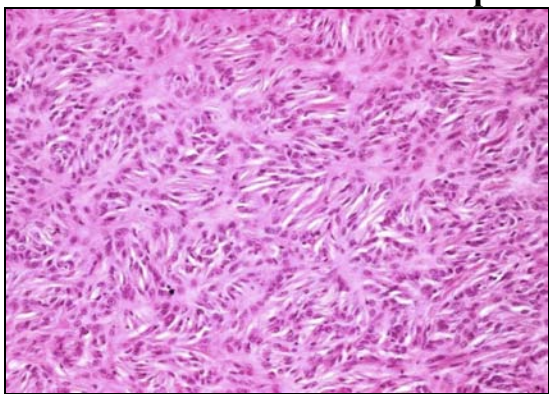

Fig. 10a: T2015/00. Neurofibrosarcoma. Palisading spindle-shaped cells with fine, wavy fibers. HE. (Obj.: 20X), dog.

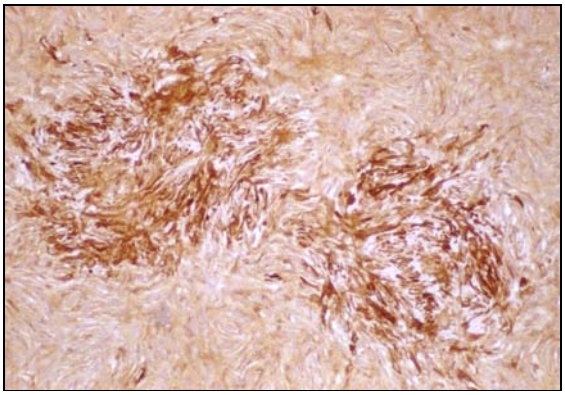

Fig. 10b: T2015/00. Neurofibrosarcoma. Immunoperoxidase, Aktin. (Obj.: 20X), dog.

Fig. 10c: T1552/00. Neurofibrosarcoma, nerve remnant. Immunoperoxidase, Neurofilament. (Obj.: 10X), dog.

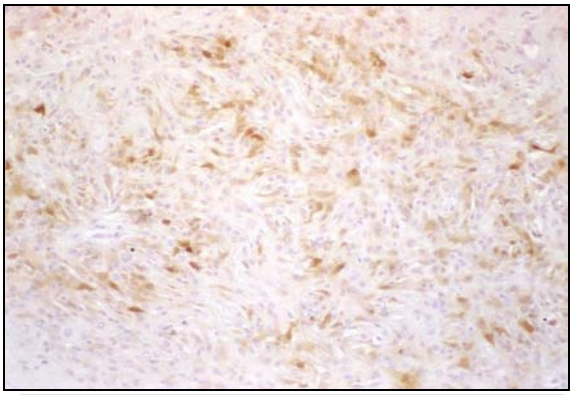

Fig. 10d: T2015/00. Neurofibrosarcoma. Immunoperoxidase, S100. (Obj.: 20X), dog.

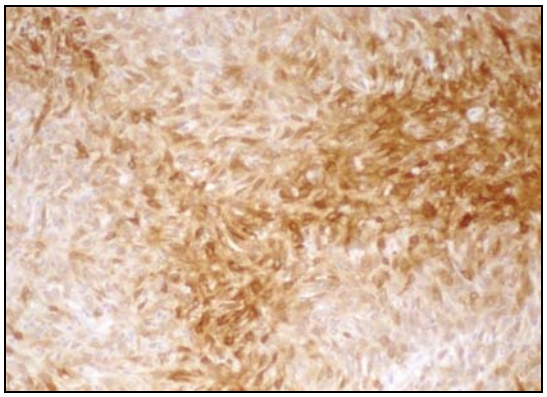

Fig. 10e: T2015/00. Neurofibrosarcoma. Immunoperoxidase, NSE. (Obj.: 20X), dog.

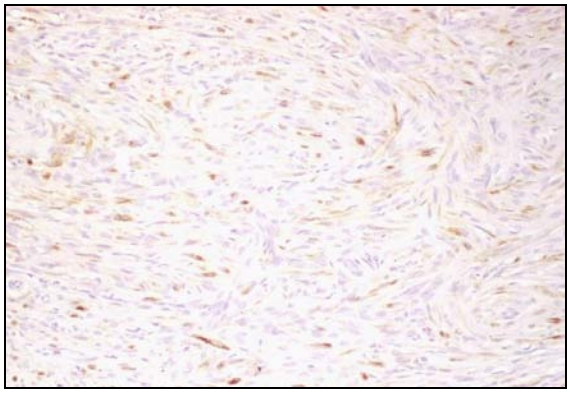

Fig. 10f: T1552/00. Neurofibrosarcoma. Immunoperoxidase,GFAP. (Obj.: 20X), dog.

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Monier A. Mohamed Sharif

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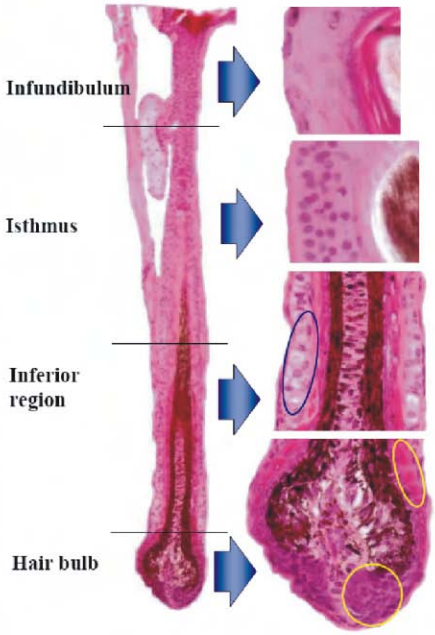

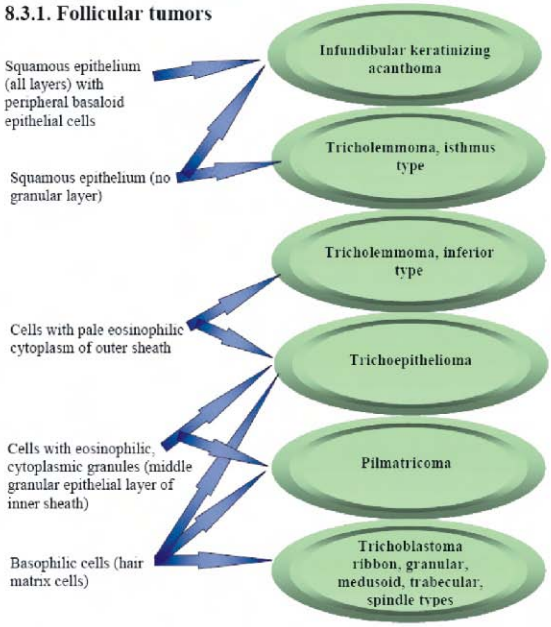

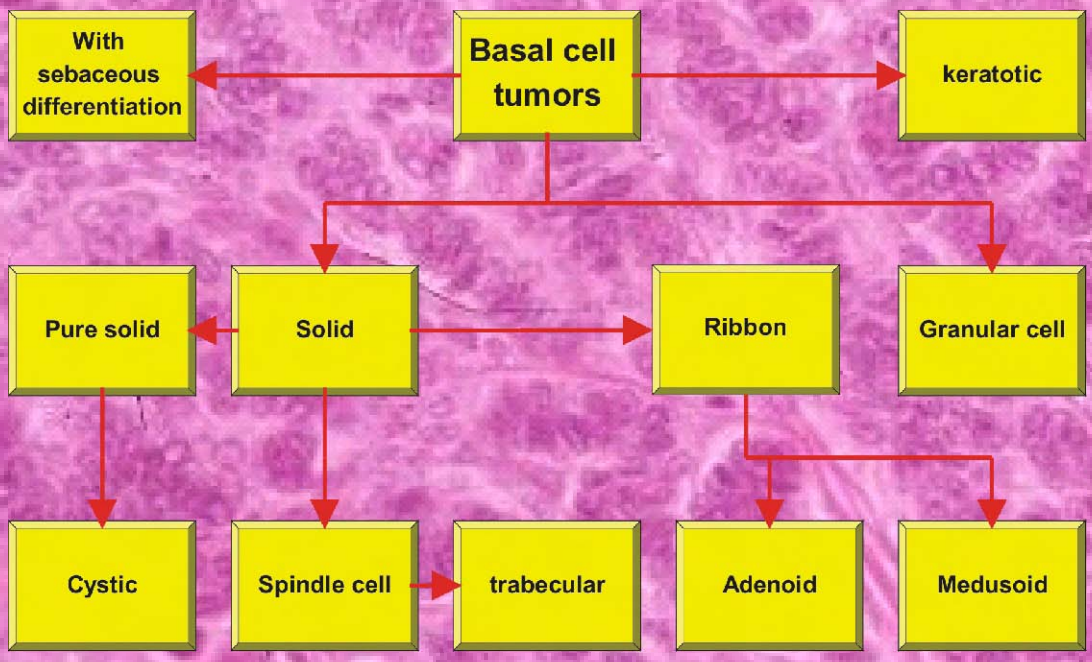

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