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# Proliferative otitis externa and the correlation to Glucocorticoids

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# 1. Introduction

Otitis externa, a prevalent condition affecting 10-20% of dogs and 2-6% of cats, presents a significant challenge in veterinary medicine. Its pathogenesis is a complex combination of predisposing factors, such as breed-specific ear canal anatomy (e.g., pendulous pinnae in Cocker Spaniels, stenotic canals in Shar Peis), environmental influences (e.g., moisture, allergens), and primary causes including hypersensitivities (atopic dermatitis being particularly prevalent), foreign bodies, parasitic infestations (Otodectes cynotis), and keratinization disorders. If not managed properly these factors often lead to a chronic, proliferative form of otitis externa characterized by significant histological alterations, including epidermal hyperplasia, sebaceous gland changes, and inflammatory cell infiltration. It is crucial in otitis externa to diagnose and manage the underlying causes early to prevent the disease getting chronic. While glucocorticoids are commonly incorporated into treatment regimens to manage inflammation and pruritus, their effectiveness varies considerably, and a broad understanding of the correlation between histopathological features and glucocorticoid response remains incomplete. This thesis aims to address this knowledge gap by undertaking a histopathological analysis of a cohort of proliferative otitis externa cases. The study will meticulously characterize the histological alterations observed, establishing a correlation between specific pathological findings and the efficacy of glucocorticoid therapy in achieving clinical improvement.

## 2. Anatomy of the ear

The ear is an organ which is responsible for hearing and the balance. It is divided into three parts, the inner ear, middle ear and external ear.

The external ear includes the pinna, a well-defined cartilaginous auricle covered by skin and fur, and the ear canal. It is shaped according to its task, to capture sound waves and transmit them through the ear canal to the eardrum. The Pinna can be moved by muscles. In comparison to humans the ear canal of dogs is much deeper and creates a better funnel to transmit sound. This leads to a better hearing ability where a dog has a about 4 times better hearing than an average person [1]. The external ear canal is curved in a S- shape toward the tympanic membrane. It can be divided into two parts, the cartilaginous outer 1/3 part of the canal and the inner bony 2/3 [2].

Through the auditory tube the tympanic cavity is connected to the pharynx, which is close to the tympanic membrane and allows air entering the middle ear. The sound conducting ossicles sit in the middle ear and transmit vibrations from the eardrum to the inner ear. This structure, consisting of a chain of three small bones, the hammer, anvil and stirrup, that sit in the air-filled middle ear.

The inner ear (*auris interna*) consists of the cochlea, the organ of hearing, and the vestibular system, the organ of balance. It consists of a membranous labyrinth within a bony labyrinth [3]. (Figure 1)

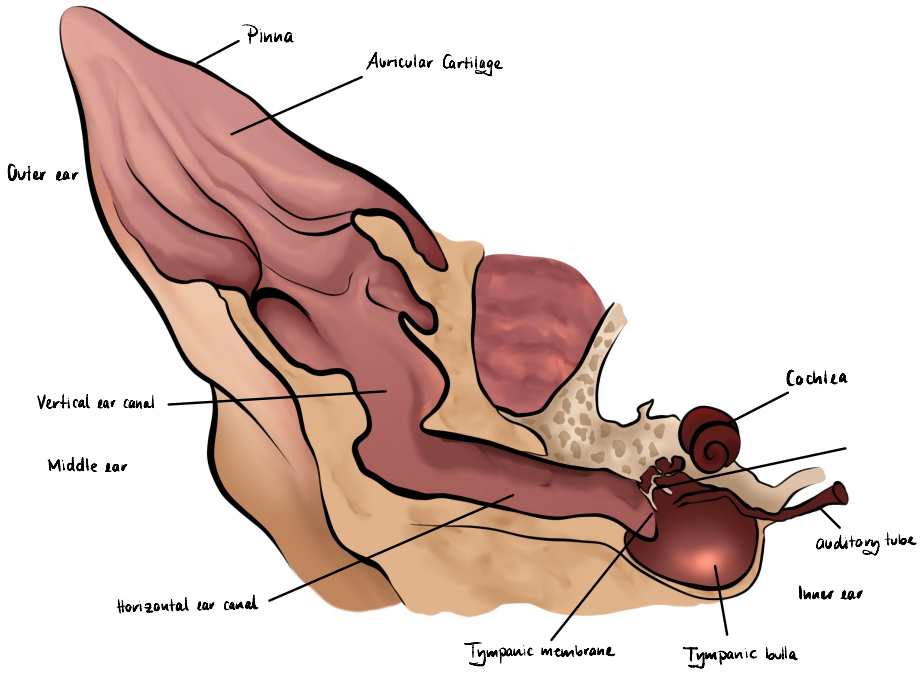


*Figure 1* Anatomy of the ear

# 3. Histology of the ear

The pinna is a structure made out of an elastic cartilage, the form of which varies greatly in dogs due to selective breeding [4]. This cartilage is surrounded by skin and covered with fur, which is connected by the perichondrium [5]. The concave surface of the ear is different from the convex side, which has similar hair than the rest of the head, whereas hair on the concave side is similar to that of the external ear canal [4]. The vertical external ear canal is majorly built by a half-ring-shaped elastic cartilage in which there lies the anular cartilage, forming the horizontal ear canal. This structure is connected to the *Anulus tympanicus* of the *Os petrosum.*

A multiple layer keratinized stratified squamous epithelium line the external ear canal including the surface of tympanic membrane facing the external ear canal [4]. While the outer part of the external ear canal usually has a small amount of protective hairs, the deeper horizontal part has a significantly lower amount of hair follicles (except for hirsute eared canines). The skin of the external ear canal contains two main types of glands, sebaceous glands and modified apocrine tubular glands (ceruminous glands) [4]. The glands are integrated into the Lamina propria [6]. The tympanic membrane is made up of three layers. The outer (distal) layer is the epidermal covering layer (*Stratum cutaneum*), the middle layer consists of connective tissue (*Stratum proprium*) and the inner (proximal) layer is the surface facing the middle ear (*Stratum mucosum*) [4][5]. The tympanic membrane is a structure made out of two parts. The dorsal *Pars flacida*, which is shimmering pink with small vessels in it, and the *Pars tensa*, which is thin, translucent, whitish [6]. The tympanic membrane's function is the transmission of the sound from the external ear canal to the middle ear and at the same time it functions as a barrer between these two areas.

# 4. Otitis externa

Otitis externa is a symptom of underlying disease rather than a diagnosis. Bacteria and yeast worsen the condition but are not primary causes. The pathogenesis is multifactorial, involving predisposing, primary, and perpetuating factors. Atopic dermatitis is a common primary cause, and failure to address the root cause often leads to treatment failure and disease progression. Proper diagnosis and treatment of the underlying cause are crucial for successful management. Inadequate response to treatment often leads to chronic, painful conditions that worsen over time. The key to managing this disease is identifying and treating all contributing factors early [2].

## 4.1 Pathophysiology

In case of Otitis externa, the inflammation of the external ear leads to skin erythema and edema [7]. Due to the swelling of the ear canal as a result of the edema the canal becomes narrow (stenosis). In early chronic cases histopathological analysis demonstrated epidermal hyperplasia. The sebaceous glands become enlarged and overactive, and the amount of inflammatory cells in the dermis and epidermis increase [6].

In the event of unsuccessful preliminary treatment, the proliferative changes continue, and the ear canal becomes further narrowed. If the condition is allowed to worsen, the histopathological changes progress and the sebaceous glands start to degenerate. Sebaceous glands undergo degenerative changes, ultimately becoming elongated and filled with a colloid mass, lacking a discernible cellular lining [6].

Apocrine sweat glands become distended and become sac-like. These glands are filled with colloidal matter mainly consisting of cellular debris [8]. The occlusion of ductal openings by keratinous and secretory debris and their hyperplasia, along with dilated apocrine glands displacing and potentially degenerating sebaceous glands, initiates a substantial inflammatory response with epidermal and dermal infiltrates. Subcutaneous thickening secondary to inflammation may ultimately result in the occlusion of the external auditory canal [6].

Sebaceous gland secretions dominate buildup of the discharge in the early stages, however the secretory function of these glands diminishes with disease progression.

The progression of chronic inflammation eventually leads to calcification and ossification of the auricular cartilage [8].

## 4.2 Clinical signs

Otitis externa is an acute or chronic inflammation of the external ear canal and includes the pinna, and the external wall of the tympanic membrane. It is a common problem in dogs and less common in cats, affecting 10-20% of dogs and 2-6% of cats [9][2]. In about a third of patients the condition is chronic. Otitis externa can be either unilateral or bilateral [10]. In case of a unilateral infection there is a higher probability for a foreign body as the underlying cause, but allergies cannot be excluded. On the other hand bilateral otitis externa is more likely to be caused by systemic disease or parasitosis [11]. In many cases the clinical signs of otitis externa may be similar and will become more severe while becoming more chronic [11].

In acute cases of otitis externa, the affected animal may start scratching and shaking its head and rubbing the head on the floor due to the pruritus and irritation of the ear canal. This can lead to erythema, alopecia or excoriation [9][11]. Signs of Inflammation in chronic cases can be visible though said erythema or oedema of the skin, increased temperature of the affected ear and pain [7]. In severe chronic otitis reduction or complete loss of hearing can also occur, due to the stenosis of the ear canal, damage to the tympanic membrane and chronic infection to the middle ear, all of which are common complications of chronic, untreated otitis externa [11]. Chronic inflammation of the external ear leads to degenerative and dysplastic changes within the soft tissue of the ear canal, eventually leading to mineralization and calcification [11].

In Otitis externa, inflammation of the skin results in the overexcitation of ceruminous glands, resulting in an excessive production of thick, brownish cerumen and pruritus is a persistent sign [10]. Dark exudate usually indicates ear mites or yeast infection. In case of secondary bacterial infection, purulent discharge may also be visible. This ‘ulcerative-purulent’ form is considered to be painful which may lead to aggressive behavior of the patients. It should be noted, that any change to the physiologic, slightly yellowish color in the cerumen may indicate infection [7][6][10]. The color of the cerumen may indicate the type of infection however it should not be used for a diagnosis. Cytology and culture and sensitivity examinations are required to identify underlying pathogens and their roles in the inflammation

There are dog breeds that are predisposed to otitis externa. One affected breed is the Cocker Spaniels where the increased amount of soft tissue, and different structure of hair follicles make the ear canal a good site for *Pseudomonas aeruginosa* growth. Other breeds that can also commonly be affected are Labrador Retrievers and Golden Retrievers [12].

Other breeds that also show a strong predisposition can be Shar Pei, Poodle, German shepherd, boxer, all kind of Spaniels, and West Highland white terriers. This can be in relation with hirsute, narrow or underdeveloped ear canals, or a predisposition to atopic dermatitis [9][13].

# 5. Etiology of otitis externa

## 5.1 Predisposing factors

Predisposing factors are causes that increase the risk of developing Otitis externa. The interaction with primary or secondary factors can eventually lead to the clinical disease [11]. In most cases these predisposing factors will change the microenvironment of the ear canal and therefore promote opportunistic behavior in microbes [14].

### 5.1.1 Conformation

The most common predisposing factor is the shape and structure of the ear canal. Dogs with genetically stenotic ear canals, as example Shar Pei-s are predisposed to ear disease, as well as breeds with an increased amount of hair in the ear canal, as can be seen in Poodles [14]. Another conformation that predisposes to infection is a pendulous pinna, such as in case of Cocker Spaniels. Even though these features can predispose to the disease it does not correlate with the disease [11].

### 5.1.2 Moisture

In case of excessive moisture accumulation in the external ear canal the Stratum corneum gets softened compromising barrier function [11]. Frequent swimming or bathing can lead to the buildup of water in the ear canal [9]. This can lead to secondary infection, and opportunistic behavior from the microorganism from the natural microflora. The frequent shifts in the moisture of the ear canal, through swimming often or through bathing/grooming, can lead subsequently to Otitis externa [11].

Similar effects can also be caused by water-based cleansers and topical aqueous antibiotic solution. It has also be suggested that environmental temperature and humidity can lead changes in the ear canal [9].

### 5.1.3 Obstructive ear disease

A partial or complete obstruction of the ear canal be it neoplastic (which is also a primary factor) stenotic (perpetuating factor) or congenital (predisposing factor), the microflora of the ear can change, which in turn also predisposes to infection and Otitis [9]. Obstructive processes also perpetuate the disease by limiting or preventing drainage of cerumen or

discharge [11]. This does not mean that every growth in the ear will lead to ear disease. Many dogs tolerate benign, slow-growing lesions without signs of an ear infection [9].

#### 5.1.4 Systemic disease

Diseases that cause a general weakening of the immune system can predispose to infections and therefore to Otitis externa. Normally these systemic diseases are not a primary cause for Otitis, but rater predispose to the infection [9]. Any disease which my decrease the efficacy of the immune system can potentially predispose to Otitis externa. According to literature, diseases like feline immunodeficiency virus (FIV), feline leukemia virus (FLV), canine parvovirus, and canine distemper may have a role in leading to Otitis externa [15].

#### 5.1.5 Iatrogenic effects

Iatrogenic damage to the ear canal due to inappropriate choice in topical treatments or excessive cleaning with dry cotton wool or traumatic removal of hair can predispose to Otitis externa. Unfortunately, the wrong choice of treatment can damage the ear canal and subsequently increase the risk of infection [11].

### 5.2 Primary Causes

Factors that themselves cause Otitis externa are called primary causes. For successful long-term therapy it is essential to identify the primary causes and treat them. Due to the ear canal being the extension of the skin, primary causes are often skin related diseases [14].

#### 5.2.1 Hypersensitivities

Skin diseases due to allergic reaction are the most common causes of chronic otitis externa. Given prevalence of atopy and the frequent association of otitis with atopic diseases, otitis externa is more commonly linked to atopy than to food hypersensitivity [14].

##### 5.2.1.1 Atopic dermatitis

Atopic dermatitis is a very common primary trigger for otitis externa [9]. It is a hypersensitivity reaction of genetically predisposed animals to inhaled or cutaneous absorbed environmental allergens. This disease can be a seasonal disease, depending on the allergen [16]. Several studies have shown that around 75% of cases of otitis externa have shown the underlying cause to be atopic dermatitis [9]. In 50% of atopic dogs, bilateral

pruritic otitis externa occurs. At the beginning of the disease the inner side of the pinnae and the ear canals only show mild erythema with no exudate. At this time clinical signs shown by the animal (scratching and head shaking), may appear severe in comparison to the changes seen in the ear canal. Pruritus is present in a small number of dogs but is only limited to the ear canal [17]. Secondary skin infections are often a result of self-trauma caused by intensive scratching [16].

#### 5.2.1.2 Food hypersensitivity

While Otitis externa is more frequently observed in atopy than in food hypersensitivity, it is notable that 80% of dogs and cats with food allergies can develop ear disease. Furthermore, in more than 20% of dogs with food allergies, ear disease may be the only discernible clinical sign [14]. Otitis externa caused by food hypersensitivity is frequently seen in young dogs, mainly younger than 6 to 9 months of age [9][14]. Regardless, the disease can occur at any time, even in dogs that have eaten the same food for years [16]. The clinical appearance is nonseasonal pruritus and can be regional or generalized. The skin involved is frequently erythematous and may have papular rash [16]. A common clinical sign in cats with food hypersensitivity is intense facial pruritus, with or without the head and ear involved.

#### 5.2.1.3 Contact allergy

Allergic contact dermatitis is a rare cause of Otitis externa. It is a type IV hypersensitivity reaction, and the changes observed are inflammation and pruritus of the commonly hairless concave aspect of the pinnae. These lesions are not only limited to the ear, similar lesions can be observed on other parts of the body, such as ventral, interdigital skin regions, inguinal and axillary skin, perianal region, perineum, ventral tail base region, and scrotum or vulva. While Atopic dermatitis or food allergy which first start itching and develop into erythema, in allergic contact dermatitis erythema is first developed, and the itching comes later. Allergic contact dermatitis reactions, along with irritant and other immunologic contact dermatitis reactions, are observed with greater frequency in cases of chronic otitis externa in dogs, primarily due to reactions to topically applied medications. In case a patient feels an increased discomfort or pain after the use of a topical medication, contact allergic reaction should be suspected [11].

### 5.2.2 Foreign body

A foreign body can be anything that causes obstruction or can irritate the ear canal [14]. During the foxtail season, plant awns frequently get lodged in the external ear canal and acr as a trigger for otitis externa. These plant parts are capable of migrating in the body and are able to reach the horizontal ear canal or rupture the tympanum [11]. Other material such as dirt or sand, small toys, lose or cross-lodged hairs, dried otic medication, and impacted wax or dead insects can also act as foreign body. Foreign bodies typically present as acute, unilateral, and severely painful otitis externa, though bilateral presentations may also occur [14][11]. In case of foreign body otitis a rapid diagnosis is very important because it may lead to severe complications such as otitis media and self-inflicted trauma [9].

### 5.2.3 Parasites

#### 5.2.3.1 Ear mites

*Otodectes sp*. are parasites that inhabit the ear canal and causes otoacariasis in cats and dogs. A few numbers of mites can cause acute discomfort due to the IgE type sensitivity reaction their secretions and skin cause. *Otodectes cynotis* is an obligatory parasitic mite that resides on the skin within the ear canal, where it is shielded by a thick layer of debris [17]. At the beginning the exudate is normally dark brown to black color but in chronic cases it may become infected by secondary infection and the exudate can become more ceruminous or purulent [11][18]. Due to scratching secondary alopecia and excoriation on the ears and head can occur and head shaking might lead to aural hematoma [18]. In cats ear mites are responsible for about 50% of otitis externa, while in dogs they make up 5 to 10% of cases [11].

#### 5.2.3.2 Dermodicosis

Other parasites that can cause ceruminous otitis externa are *Dermodex canis* and *Dermodex cati* [17]. Demodicosis is a skin disease which is very contagious and often associated with underlying immunosuppressive or metabolic diseases. In feline demodicosis such diseases are feline immunodeficiency virus (FIV), feline leukemia virus (FeLV), toxoplasmosis, systemic lupus erythematosus, neoplasia, or diabetes mellitus [18]. The disease is characteristic by pruritic ceruminous otitis externa, although clinical signs frequently conenctrate on the pinna, or focal patchy alopecia and erythema which might be patchy [18].

#### 5.2.3.3 Spinous Ear Tick

The larvae of *Otobius megnini*, the spinous ear tick, causeinflammation by attaching to the lining in the external ear canal. Infection with Otobius megnini occurs more frequently in dogs and less in cats [17]. Clinical appearance include waxy exudate, strong head shaking, and ear scratching [18].

Additional parasites that trigger inflammation and itching on or near the pinnae, which can result in head shaking and scratching, thereby contributing to secondary otitis externa, include *Sarcoptes scabiei*, *Notoedres cati*, *Cheyletiella spp*., and *Eutrombicula spp*. [11].

### 5.2.4 Keratinization disorders

The alteration of keratinization and cerumen gland function in the external ear canal can have many different reasons. Endocrine disorders, like hypothyroidism, hyperadrenocorticism, and sex-hormone imbalance can be causes to such changes and leading to an initial ceruminous and seborrheic form of otitis externa [11]. Otitis resulting from endocrine disorders, such as gland dysfunction, is not primarily associated with pruritus; however, it frequently leads to secondary infections that can subsequently cause itching [9].

#### 5.2.4.1 Canine primary seborrhea

The keratinization disorder, Canine primary seborrhea, is a common disease in dogs. Breeds with the highest frequency are American cocker spaniels, English springer spaniels, West Highland white terriers, and basset hounds. The clinical signs start in juvenile dogs with mild symptoms that get worse with aging. The signs shown are a dull, dry hair coat, increased scaling, scaly and crusty seborrheic patches. Secondary ear infection with bacteria and fungi are very common [19].

#### 5.2.4.2 Facial dermatosis of Persians

Facial dermatitis of Persian cats is an uncommon disease of unclear cause. It most commonly affects older kittens and young adult cats. The clinical appearance is black, waxy debris around the eyes or mouth or on the chin. Over time, the lesions become increasingly inflamed and pruritic. The condition may also involve both ears, resulting in bilateral ceruminous

otitis externa, and the face, seborrheic facial dermatitis, and often leads to secondary yeast infections [19].

#### 5.2.4.3 Sebaceous adenitis

Sebacious adenitis usually manifests, when affecting the ears as dry, scaly ears and mild inflammation. Usually these clinical signs are paired with other skin involvement. This condition is rare in dogs, with highest occurrence in standard poodles, Akitas, and Samoyeds [9].

### 5.2.5 Autoimmune diseases

Autoimmune diseases of the skin that affect the concave surface of the pinna are Pemphigus vulgaris, Pemphigus foliaceus, Pemphigus erythematosus, discoid Lupus erythematosus, bullous pemphigoid, and mucous membrane pemphigoid [11]. These diseases may infect the ear canal and cause Otitis externa. Usually they are rare and if present, lesions are visible on other parts of the body [11].

#### 5.2.5.1 Pemphigus vulgaris

The autoimmune disease, Pemiphigus vulgaris, is producing autoantibodies against antigens in or near the epidermal-dermal junction, which leads to cell detachment within the deeper epidermal layers. Pemiphigus vulgaris is a rare disease of dogs and cats. The clinical appearance involves erosions, ulcers, and in rare cases vesicles and bullae on the skin, mucous membranes and mucocutaneous junctions. Other common general signs are fever, depression, and anorexia [20].

#### 5.2.5.2 Pemphigus foliaceus

Pemphigus foliaceus is one of the most common autoimmune skin diseases in dogs and cats, and any breed, age can be affected. Usually the disease is idiopathic, but it can be drug induced, or it can also be secondary to an inflammatory chronic skin disease.

Pemphigus foliaceus builds a crust and can typically be found on the head. Primary lesions are focal erythema and superficial pustules that are followed by secondary crust formation [20].

For the diagnosis of such autoimmune diseases', histopathological examination of the skin through skin biopsy is necessary. With this examination it is possible to identify the pathognomic acantholytic cells [9].

#### 5.2.5.3 Pemphigus erythematosus

This disease is an autoimmune disease that might be an overlap between pemphigus and lupus erythematosus or may be a benign form of pemphigus foliaceus. The normal clinical appearance are superficial erosions, scales, and crusts. In cats it is an uncommon disease, but common in dogs. Dog breeds that are more represented are German shepherds, collies, and Shetland sheep dogs [20].

#### 5.2.5.4 discoid Lupus erythematosus

Discoid Lupus erythematosus is a common disease in dogs and rare in cats. The clinical signs that normally appear in dogs are erythema, scaling, erosions, ulcerations and crusting on the nose bridge, lips, periocular skin and ear pinnae, rarely it involves the distal limbs or genitals. In Cats erythema, alopecia, and crusting on the face and ear pinnae are frequent signs [20].

### 5.2.6 Trauma

Trauma on the external ear canal is a rare cause of otitis externa. The trauma can happen at any time but in general the tramuatic incident may occur months or years before clinical signs appear. In many cases the underlying lesions are not recognized and can only be visualized by using computer tomography or magnetic resonance imaging (MRI) [14].

### 5.2.7 Neoplasia

Neoplastic diseases can be a cause of otitis externa in case of neoplasia of the ear. In cats ceruminous gland adenomas and adenocarcinomas, sebaceous gland adenomas and carcinomas, squamous cell carcinomas and papillomas are neoplastic growths that can cause Otitis externa. While in dogs ceruminous gland adenomas and adenocarcinomas, papillomas, basal cell carcinomas, squamous cell carcinomas are the usual neoplasia in connection with otitis externa [21][22].

## 5.3 Perpetuating Causes

Perpetuating causes are factors that maintain or worsen the inflammation in the ear canal and when not adressed, are often a main cause for treatment failure [11]. The change of the environment of the external ear leads to opportunistic infection [17]. Perpetuating factors include infection of bacteria and yeast, progressive pathological changes, as a result of chronic inflammation, excessive amounts of discharge and Otitis media [11].

### 5.3.1 Bacterial infection

The microflora of the normal external ear canal contains low numbers of a variety of symbiotic and possibly pathogenic bacteria. This is the reason why bacteria cultured from an ear swab cannot be assigned a causative role of otitis externa without cytological examination [17]. Since bacterial infection is a secondary cause of otitis externa, bacterial otitis externa is only a partial diagnosis [14]. In case the microclimate of the external ear canal is altered these bacteria will colonize quickly, worsen the proliferation and lead to maintaining the inflammation of the ear canal [17].

The most common symbiotic bacteria that can be cultured from a normal canine ears are *Staphylococcus sp*., *Micrococcus sp*., and, coliforms [15]. Under normal conditions less bacteria are on the microflora of the external ear canal [11].

In case otitis externa has developed the most common bacterial species are *Staphylococcus pseudintermedius*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Escherichia coli*, *Corynebacterium spp.*, *Enterococcus spp*. and *Streptococcus* spp. [23].

Coagulase-positive Staphylococcus pseudintermedius, S. aureus, and S. schleiferi subsp. coagulans, along with coagulase-negative S. epidermidis, S. schleiferi subsp. schleiferi, S. simulans, and S. saprophyticus, are the primary staphylococcal species associated with this condition [24].

### 5.3.2 Yeast infection

Like bacteria, yeasts in low numbers have a natural inhibitor role in the ear canal. They can be found in the normal ear of almost 50% of dogs and almost 25% of cats [14][11].

In animals that are continuously under antibiotic treatment, Yeast overpopulation and secondary infection is expected [24]. Yeasts replicate under favorable conditions which are provided by the primary diseases that cause inflammation and increased sebum production

and leading to microbial overgrowth [24][25]. The most common yeasts that cause infection of the ear are *Malassezia pachydermatis* and occasionally *Candida spp*. [11].

In dogs *Malassezia* induced inflammation usually affects the parts of the body with an increased relative humidity and are usually associated with atopic dermatitis or food hypersensitivity. Patients with *Malassezia* infection of the external ear generally show a severely inflamed ear [25]. The clinical appearance of fungal infection is moderate to severe pruritus, and in case of chronic cases, the becoming hyperpigmented, lichenified, and pinnae hyperkeratosis [22].

The infection is common in dogs , especially among West Highland white terriers, dachshunds, English setters, Basset hounds, American cocker spaniels, shih tzus, Springer spaniels, and German shepherds, and rare in cats [25][26]. In Cats clinical signs include black waxy ears, multifocal to generalized erythema and seborrhea [26].

### 5.3.3 Otitis media

The extension of infection through the tympanic membrane from the external ear to the middle ear is the most common cause of the inflammation of the middle ear (otitis media) [14]. Inflammation and infection of the middle ear is an important perpetuating factor for Otitis externa [17]. In case of reoccurring otitis externa or a chronic case, it should be considered that the condition could originate from the middle ear and could be a possible cause even with an intact tympanic membrane [14]. The infection is either a descending infection through the ruptured tympanic membrane or ascending through the Eustachian tube from the nasal cavity [11]. The main pathogens that can be isolated from an infected middle ear are Staphylococcus pseudintermedius, Pseudomonas and yeasts [24].

### 5.3.4 Progressive Pathologic Changes

The Result of chronic otitis externa and otitis media can result in advanced chronic proliferative processes that lead to end-stage otitis. Progressive changes may affect the external ear canal walls or tympanum [9]. In case the pathological changes are so far advanced that the conservative treatment does not show any success, surgical intervention is needed [27].

# 6. Therapeutic aspects

Early recognition of chronic pathological changes is very important for the treatment and the long-term outcome. It is important to know that the more severe the changes are, the harder it is to treat. This is the reason why it is important to assess the pathological changes in order to decide on the treatment [28]. Acute otitis externa can be managed in most cases with the use of polyvalent topical ear products that combine a glucocorticoid, antimicrobial and an antifungal. In case of chronic proliferative otitis externa the treatment is a bigger challenge [28][29]. The correct diagnosis and treatment of the underlying factors leading to persistent otitis and treating the inflammatory changes are key points in successfully treating chronic otitis externa. The most commonly used therapeutic method is the use of topical medication. In most cases it is benefitial to use an additional anti-inflammatory drug [30].

## 6.1 Cleaning

After the identification and treatment of the primary cause(s), and if possible, the improvement of the predisposing factors, the removal of debris and discharge may help treat otitis externa. Biofilms have a major impact on antimicrobial resistance and therefore on treatment. This mucous, thick discharge is often dark brown or blackish, and may hide bacteria and cells. As literature suggests biofilms inhibit cleaning, prevent penetration of antimicrobials and provide a protected reservoir of bacteria. Especially in Gram-negative bacteria, biofilms may increase the development of antimicrobial resistance [29][30].

Bacteria will be exposed to either high or low concentration of antimicrobials, which greatly affects treatment outcomes. Those bacteria that are not eliminated due to the inadequate local dose of the antibiotic will lead to treatment failure as they build a reservoir in the biofilm, although their resistance is relatively low [29]. The cleaning of the ear before using topical therapy is therefore crutial for effective topical treatment. The cleaning of a healty ear is not nessecary and if done, may favor the development of ear diseases. In case of ears that tend to produce a lot of cerumen a routine cleaning of the ear can be helpful. In case of increased amounts of hair in the ear canal the hair should be removed during anaesthesia [31]. The total cleaning of hair, cerumen, exudates and foreign bodies from the external ear canal and the pinnae is essential to give complete visual access to the ear canal and to identify the tympanic membrane, futehermore, with proper ear cleaning additional inflammatory processes are minimalized, and the topical therapy is able to reach the epidermis [31][32].

## 6.2 Topical therapy

If possible, the choice of a topical therapy is the preferred method of treatment. Cytological and otoscopic analysis is helpful in finding the right therapeutic method and to evaluate the response of the treatment. Frequent reevaluation is important to decide if changes in treatment are necessary [29][30].

### 6.2.1 Antibiotics

Antibiotic therapy should always be the performed indicated by a cytological examination followed up by bacterial culture and sensitivity [32]. For most bacterial infections polymyxin B, fusidic acid, florfenicol, gentamicin, enrofloxacin and marbofloxacin are effective. Against pseudomonas infection fluoroquinolones, gentamicin and polymyxin B are generally effective. In case of methicillin-resistant Staphylococcus aureus and methicillin-resistant Staphylococcus pseudintermedius adequate treatment options may befusidic acid and florfenicol [29].

In case of gram-negative pathogens an antibiogram should be done. In many cases polypeptide-antibiotics like polymyxin B are used [32]. Aminoglycoside and polymyxin B are potent ototoxic drugs that could damage the inner ear which could lead to loss of hearing. These drugs should not be used in case of damage to the tympanic membrane [32][29].

### 6.2.2 Antifungals

For the treatment of yeast infection only effective antifungal medications should be used, to which sensitivity was confirmed. Against *P. canis* nystatin, miconazole and thiabendazole are highly [10]. Other effective products are ketoconazole or clotrimazole. The antifungal-containing ear preparations should be administrated with a dropper bottle, brown-amber bottle, or something that offers accurate dosing. The treatment should be done until on the follow-up the ear canal epithelium has normalized and is no longer edematous or inflamed, and cell and microbe counts in ear smears are within normal limits [22]. The adequate volume of the preparation is very important for proper penetration [29].

## 6.3 Systemic therapy

In suppurative otitis externa systemic treatment might be more beneficial due to the active inflammatory discharge in the deep ear canal tissues, and possibly the middle ear. In most cases where topical treatment cannot be used systemic therapy is indicated [29]. It must be

considered that systemic antibiotics might be useless in case of cerumen and pus that contains bacteria [10].

Good first line drugs for staphylococcus infection are clindamycin, lindomycin, cefadroxil, cefalexin and clavulanate- potentiated amoxicillin. Second line choices are fluoroquinolones, for these it is important to have culture evidence that the first-line drugs are not affective [29].

### 6.4 Glucocorticoids

In most dogs with otitis externa the patients benefit from anti-inflammatory therapy either on its own or additionally to antimicrobial therapy. The reduction of pain and swelling by using glucocorticoids for a short duration may help with improving ear self-cleaning and medication administration [30][10]. They help to reduce proliferative reactions and pruritus [10]. The dermal ulceration caused by pseudomonas infection can be reversed by Glucocorticoids [10].

#### 6.4.1 Topical glucocorticoids

Topical glucocorticoids combined into ear medications can be used for the treatment of acute otitis externa. Mild pruritus can be treated by using low potency topical glucocorticoids,while more severe pruritus needs long term treatment with more potent products. Severe bacterial infections should not be treated with very potent products due to the suppression of neutrophil activity. Topical glucocorticoids should be used at the lowest frequency that controls pruritus [29].

#### 6.4.2 Systemic glucocorticoids

To control pruritus and stenosis prednisolone or methylprednisolone can be used for one to three weeks. In case of severe fibrosis and stenosis, betamethasone or dexamethasone are more effective, around 7.5 to 10 times more potent than prednisolone [29].

Prednisolone, methylprednisolone or ciclosporin are used at the lowest frequency and dose is used for long-term treatment to prevent recurrence of otitis externa [29].

# 7. Materials and methods

A total of 6 dogs were selected with signs of chronic otitis externa and at least moderate levels of otic proliferation. All dogs were patients of the ambulatory otological practice, as well as the patients of the endoscopic department of the Department of Internal Medicine, University of Veterinary Medicine, Budapest.

In order to evaluate the degree of inflammation and proliferation a scaling system was used where the following parameters were evaluated: pinnal skin proliferation, ear canal diameter, ear canal skin proliferation, discharge, and state of tympanic membrane. Type of glucorticoid used, additional treatments were also recorded as well as day differences in different evaluations, starting at T0. These were assessed before and after treatment using a standardized scoring system with hyperplasia was scored from 0 (absent) to 3 (severe), proliferation was scored from 0 (absent) to 3 (severe) and Ear canal narrowing width was scored from 0 (normal) to 3 (severe) (Figure2).

Patients who had no detailed followup data were excluded. The results where then analyzed in terms of glucocorticoid used and treament efficacy.

| Left ear | | | | | | | |
|---|---|---|---|---|---|---|---|
| Patient | Time | Pinna (hyperplasia) | Ear canal skin (proliferation) | Ear canal width | Total | Glucocorticoid type | Additional Treatments |
| 289669 | 0 | 3 | 2 | 3 | 8 | Prednisone | None |
| | 53 | 0 | 1 | 2 | 3 | | Squalene ear wash |
| 261550 | 0 | 0 | 3 | 3 | 6 | Topical Dexamethasone | Marbofloxacine, Ketoconazole |
| | 120 | 0 | 1 | 1 | 2 | Repeated topical Dexamethasone | |
| 314665 | 0 | 0 | 1 | 1 | 2 | Prednisone | topical hyrdocortizone |
| | 79 | 0 | 0 | 0 | 0 | Topical Dexamethasone | Marbofloxacine, Ketoconazole |
| 314062 | 0 | 0 | 0 | 0 | 0 | Topical Dexamethasone | Marbofloxacine, Ketoconazole |
| | 14 | 0 | 0 | 0 | 0 | | |
| 321479 | 0 | 2 | 3 | 2 | 7 | Dexamethasone | Marbofloxacine, Ketoconazole |
| | 14 | 0 | 1 | 1 | 2 | | |
| 319153 | 0 | 2 | 1 | 1 | 4 | Topical hydrocortizone | chlorhexidine, TRIZ EDTA |
| | 14 | 1 | 1 | 1 | 3 | Topical hydrocortizone | |

| Right ear | | | | | | | |
|---|---|---|---|---|---|---|---|
| Patient | Time | Pinna (hyperplasia) | Ear canal skin (proliferation) | Ear canal width | Total | Glucocorticoid type | Additional Treatments |
| 289669 | 0 | 3 | 3 | 3 | 9 | Prednisone | None |
| | 53 | 0 | 0 | 1 | 1 | | Squalene ear wash |
| 261550 | 0 | 0 | 2 | 3 | 5 | Topical Dexamethasone | Marbofloxacine, Ketoconazole |
| | 120 | 0 | 0 | 0 | 0 | Repeated topical Dexamethasone | |
| 314665 | 0 | 2 | 3 | 3 | 8 | Prednisone | topical hyrdocortizone |
| | 79 | 0 | 0 | 0 | 0 | Topical Dexamethasone | Marbofloxacine, Ketoconazole |
| 314062 | 0 | 0 | 1 | 1 | 2 | Topical Dexamethasone | Marbofloxacine, Ketoconazole |
| | 14 | 0 | 1 | 1 | 2 | | |
| 321479 | 0 | 0 | 1 | 1 | 2 | Dexamethasone | Marbofloxacine, Ketoconazole |
| | 14 | 0 | 1 | 1 | 2 | | |
| 319153 | 0 | 2 | 1 | 1 | 4 | Topical hydrocortizone | chlorhexidine, TRIZ EDTA |
| | 14 | 1 | 1 | 1 | 3 | Topical hydrocortizone | |

*Figure 2* Scoring of the parameters

Hyperplasia: 0 = absent
1 = Mild
2 = Moderate
3 = Severe

Proliferation: 0 = Absent
1 = Mild
2 = Moderate
3 = Severe

Ear Canal Width: 0 = Normal
1 = Mild narrowing
2 = Moderate narrowing
3 = Severe narrowing

# 8. Results

This study evaluated the efficacy of glucocorticoid treatment in six dogs diagnosed with otitis externa. All six patients exhibited some degree of improvement following glucocorticoid treatment. One patient showed complete resolution of all clinical signs, as indicated by scores of 0 for all assessed parameters, which can be observed in figure 3 and 4. This was observed after a mean treatment duration of 79 days, with the treatment of one dose of Prednisone 0.5mg/kg at day one of treatment plus topical hydrocortisone, hyperallergenic feed and additional therapy at day 60 with topical dexamethasone, Merbofloxacine and Ketoconazole.

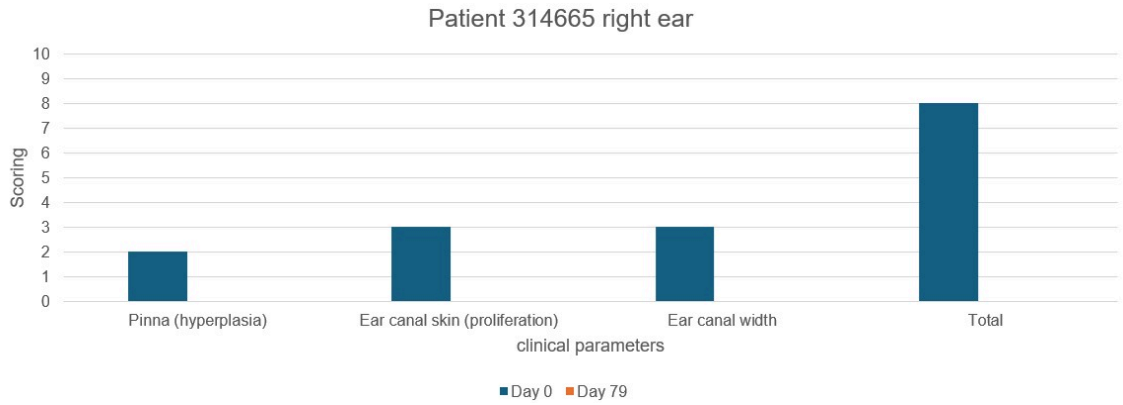


*Figure 3* Result Left ear of patient 314665

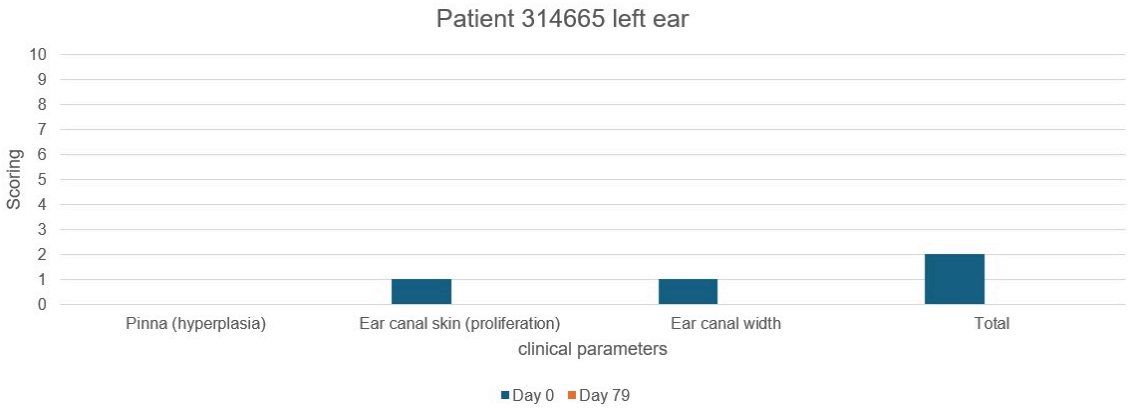


*Figure 4* Result right ear of patient 314665

Two patients showed significant improvement. One patient showed moderate improvement on the left ear with a reduction in the combined score of 8 to 3 and 9 to 1 on the right ear and with a treatment duration of 53 days. This can be seen on Figure 5 and 6. The therapy included 0.5mg/kg Prednisone on day zero, on day 16 the dose of Prednisone was reduced

to 0.25mg/kg with additional treatment with squalene ear wash. On day 53 the Prednisone was weaned off and the dog was put on hypoallergenic feed.

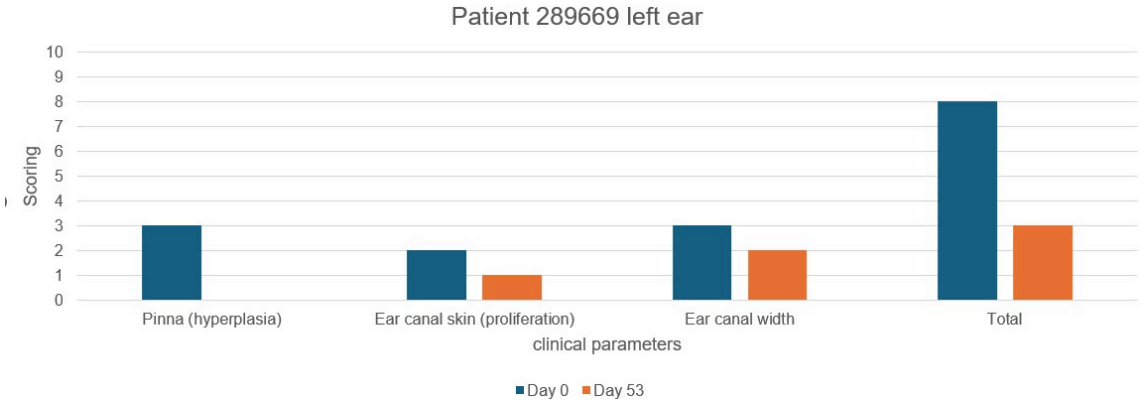


*Figure 5* Result left ear of patient 289669

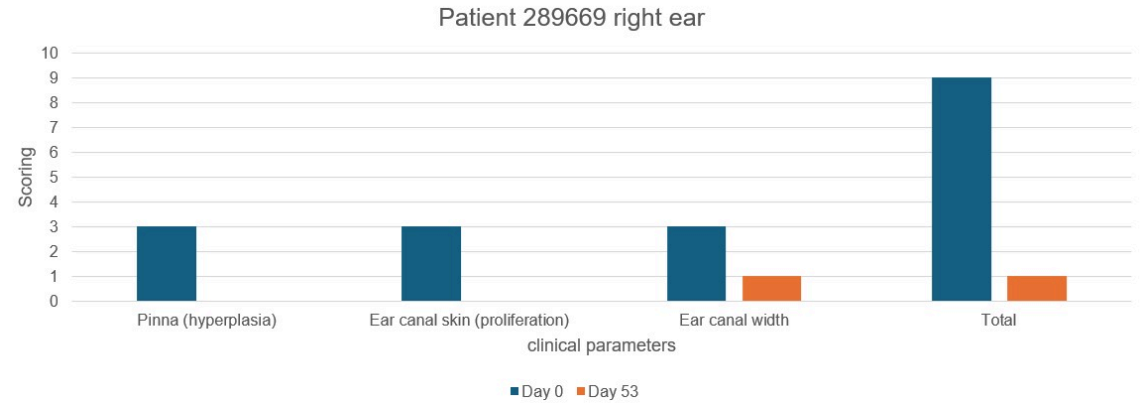


*Figure 6* Result right ear of patient 289669

The second patient with significant improvement showed a complete improvement on the right ear with a reduction of the combined score of 5 to 0 (Figure 8) and 6 to 2 on the left ear (Figure 7) with a moderate improvement. The therapy used on that patient was topical Dexamethasone on day 0 with additional treatments with Marbofloxacine and Ketoconazole, which was again repeated at day 120.

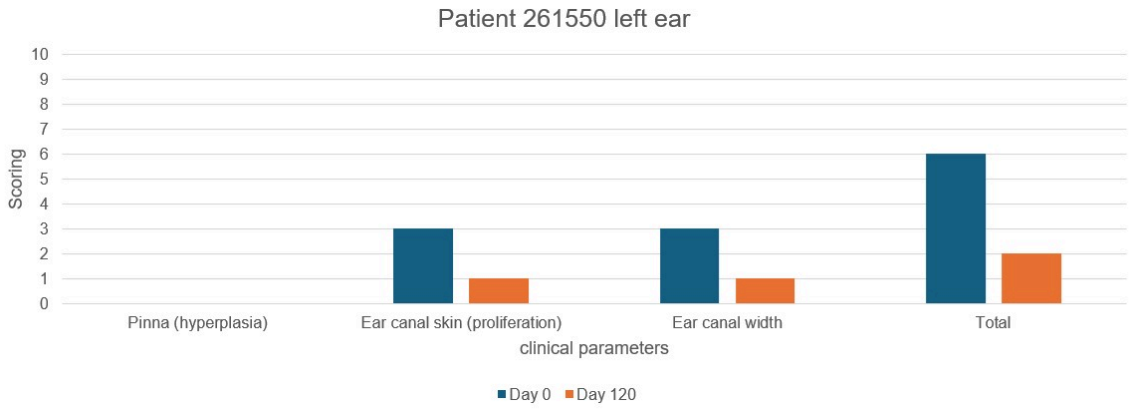


*Figure 7* Result left ear of patient 261550

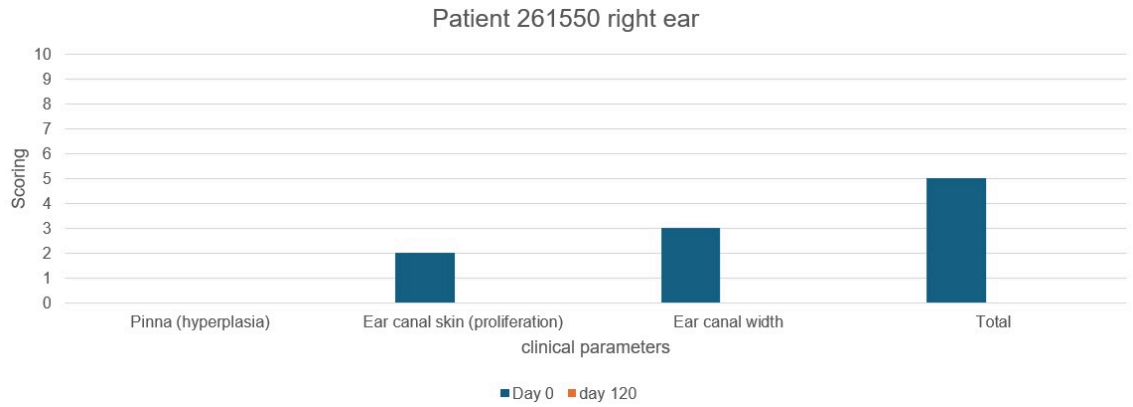


*Figure 8* Result right ear of patient 261550

One of the patients showed moderate improvement, displaying a reduction in the combined score of 7 to 2 points on the left ear (Figure 9) and stayed on score 2 with no improvement on the right ear (Figure 10). The treatment duration was 14 days with the use of topical Dexamethosone on day one plus additional treatments with Marbofloxacine, Ketoconazole and foreign body removal.

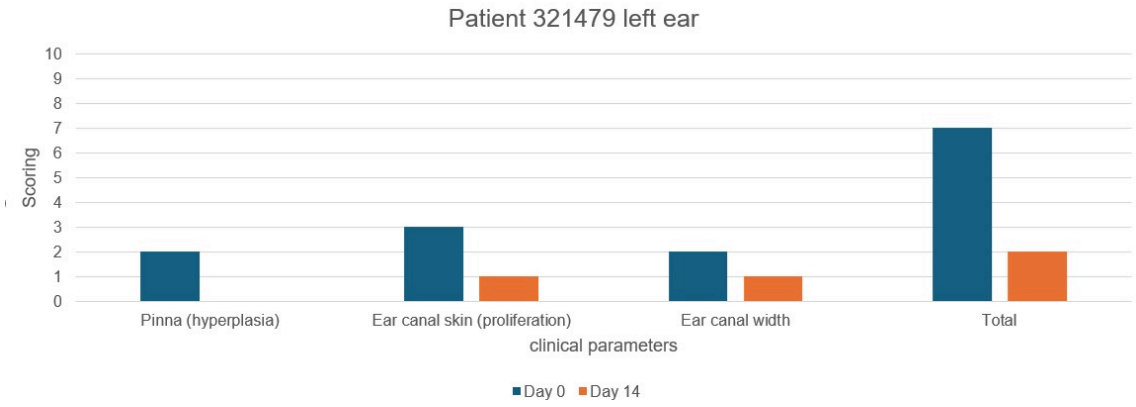


*Figure 9* Result left ear of patient 321479

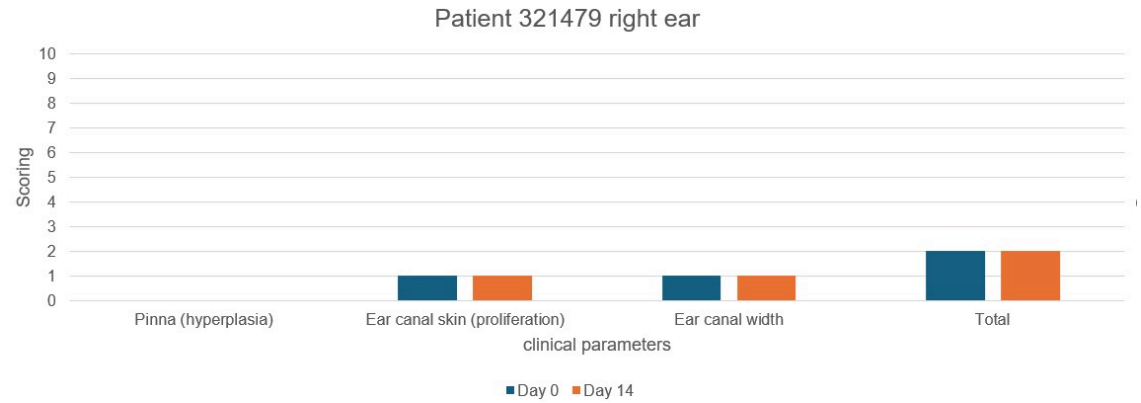


*Figure 10* Result right ear of patient 321479

One patient showed only a slight improvement with a reduction in the combined score of 4 to 3 on the left ear (Figure 11) and 4 to 3 on the right ear (Figure 12). The treatment was done over a time of 14 days with the use of topical hydrocortisone and additional treatment with chlorhexidine and TRIZ EDTA.

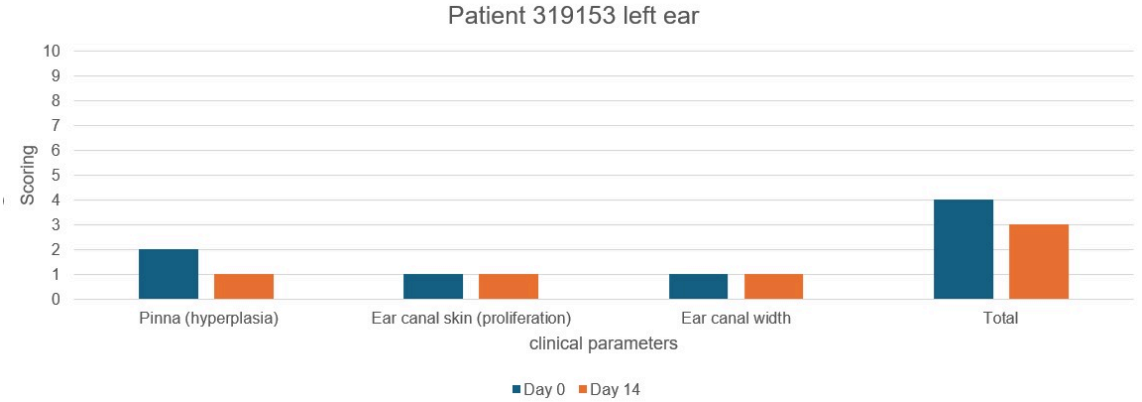


*Figure 11* Result left ear of patient 319153

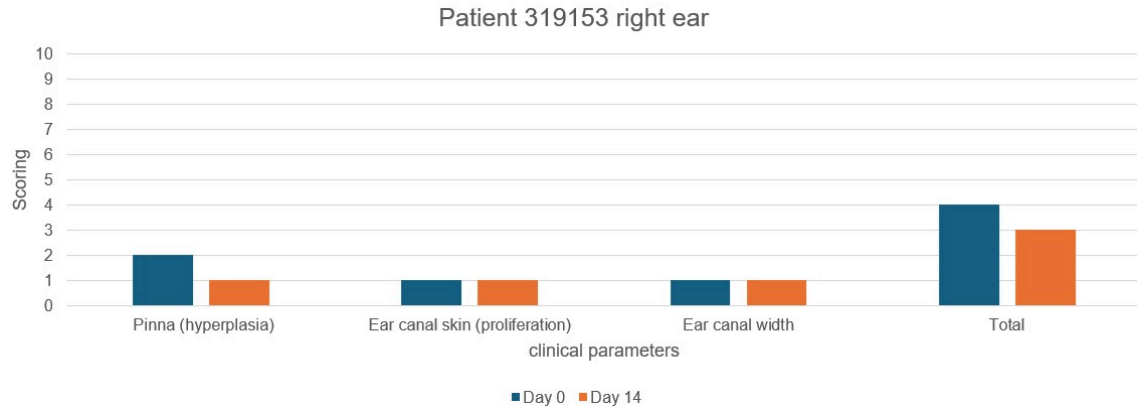


*Figure 12* Results right ear of patient 319153

Finally one patient showed no improvement in the right ear (Figure 13), while the left ear was not affected with Otitis externa, with a treatment duration of 14 days. The treatment used was topical Dexamethasone with additional treatment with Marbofloxacine, Ketoconazole and the removal of a foreign body.

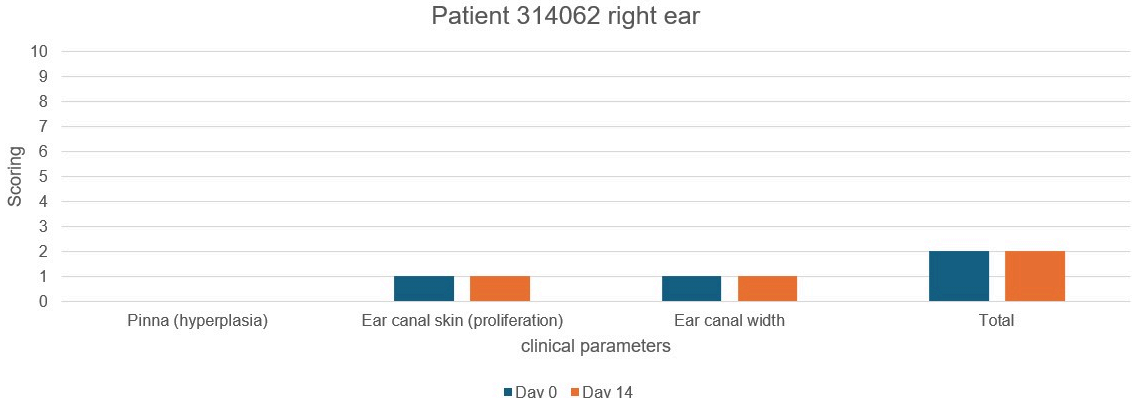


*Figure 13* Result right ear of patient 314062

# 8. Discussion

The present study investigated the efficacy of glucocorticoid therapy in alleviating clinical signs associated with proliferative otitis externa in a group of six canine patients. The results demonstrated an improvement across all parameters assessed, supporting the established role of glucocorticoids in managing the inflammatory processes of this challenging condition. However, the degree of improvement and the time required for resolution varied considerably amongst the patients, highlighting the complex and multifactorial nature of otitis externa. Consistent with the literature, the observed variability in treatment response may be attributed to several factors. The initial severity of the disease, which varied from mild to severe, influenced the overall outcome. Furthermore, the underlying causes of otitis externa likely varied among the patients. While this study did not explicitly identify primary aetiologies the literature highlights the frequent involvement of hypersensitivities (in particularly atopic dermatitis), foreign bodies, parasitic infection, and various keratinization disorders. The presence of such factors could significantly impact the effectiveness of glucocorticoid treatment. The diverse range of additional treatments administered in this study (e.g., topical antibiotics, antifungals, hypoallergenic diets, foreign body removal) underlines the necessity of addressing underlying causative factors, along with symptomatic management using glucocorticoids, for improved treatment outcomes.

This study demonstrates the significant improvement observed across the assessed parameters. However, the variability in treatment response underscores the complexity of this condition and the need for a more nuanced understanding of its pathogenesis. Future research should focus on larger, more diverse groups to confirm these findings and explore the predictive value of specific histopathological characteristics in guiding treatment decisions, potentially leading to improved clinical outcomes.

The limited sample size (n = 6) restricts the present study, potentially affecting both the statistical power to detect significant effects and the generalizability of the conclusions to broader populations.

# 9. Abstract

Otitis externa is a prevalent and often challenging condition in the veterinary practice, which, if not treated properly it can develop to a chronic, proliferative disease characterized by significant histopathological changes.

This study assessed the effectiveness of glucocorticoid therapy in six dogs with this condition, using a standardized scoring system (0-3) to evaluate three key clinical parameters: pinna hyperplasia, ear canal skin proliferation, and ear canal narrowing.

Pre- and post-treatment scores were analyzed using paired t-tests to determine the significance of treatment effects of glucocorticoids. However, inter-patient variability in response highlighted the multifactorial nature of the disease, underscoring the need for individualized treatment strategies.

The limited sample size (n =6) of this study requires further research with larger and more diverse groups. Future studies should investigate the predictive value of histopathological characteristics and refine treatment strategies with the help of a larger, more diverse group. This improved understanding could facilitate more effective and individualized management strategies for proliferative otitis externa, improving both clinical outcomes and animal welfare.

# 10. Összefoglalás

A külső hallójáratgyulladás (otitis externa) egy gyakori, terápiás kihívásokkal járó betegség az állatorvoslásban, ami, a kezelés sikertelensége esetén, idült, proliferatív, jelentős kórszövettani elváltozásokkal járó állapottá progrediálhat.

Kutatásunk a glükokortikoid terápia hatékonyságát vizsgálta hat, idült, proliferatív hallójáratgyulladásban szenvedő kutyában, egy standardizált pontozási rendszert használva a főbb klinikai paraméterek értékelésére (fülkagyló hiperplázia, bőr proliferáció, hallójárat szűkület)

Kezelés előtti és utáni pontszámokat párosított t-tesztekkel vizsgáltuk a glükokortikoid terápia hatékonyságát. A betegek közt jelentős különbségek adódtak a kezelés hatékonyságát illetően, aláhúzva a fontosságát a személyre szabott terápiának.

A limitált elemszám (n=6) miatt további kutatásra javasolt egy nagyobb és változatosabb betegpopulációval. A jövőbeli kutatásoknak a kórszövettani elváltozások prediktív hatásait is figyelembe kell venniük, a nagyobb, változatosabb populációban. Az így nyerhető magasabb szintű megértése a betegségnek jelentősen segíthetné a proliferatív otitis externa gyógykezelésének kedvező kimenetelét a jövőben.

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