

SPECIAL ISSUE REVIEW

A major review on disorders of the animal lacrimal drainage systems: Evolutionary perspectives and comparisons with humans



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ABSTRACT

Purpose: To provide a systematic review of the literature on the disorders and management of the lacrimal drainage system (LDS) in few of the species of the animal kingdom.

Methods: The authors performed a PubMed search of all articles that were published in English with specific reference to lacrimal drainage disorders in animals. Data captured include demographics, presentations, investigation, diagnoses and management modalities. Emphasis was also on anatomical differences, evolutionary perspectives and addressing the lacunae and potential directions for future research.

Results: The lacrimal drainage system is a terrestrial adaptation in vertebrates. Evolutionary development of the LDS is closely linked to the Harderian gland and the vomeronasal organ. Variable differences in the clinical presentations and management of lacrimal drainage disorders (LDD) are noted in comparison to humans. These are secondary to unique structural and pathophysiological differences. Uniformity in usage and reporting of disease terminologies is required. Diagnostic challenges in clinical examination can be met with the development of customized lacrimal instruments. Contrast dacryocystorhinography is a very useful investigation in the diagnosis of LDD. Multiple bypass procedures like conjunctivorhinostomy, conjunctivobuccostomy and conjunctivomaxillostomy have been described for nasolacrimal duct obstruction (NLDO). Advances of endoscopy and radiological techniques are paralleled by minimally invasive lacrimal interventions. The search for an ideal animal model for human LDS is far from over and the choice of the animal needs to be customized based on the research objectives.

Conclusion: The lacrimal drainage system is an ancestral feature in tetrapod vertebrates and it is present, in some form or another, in most descendant species. The lacrimal drainage system has evolved considerably, adapting to the needs of the species. It is essential to understand the lacrimal drainage disorders of domestic animals so that the animal and human lacrimal sciences contribute more meaningfully to each other.

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1. Introduction

Animal research is a vital component of medical research and has not only been used as model for disease studies but also for development and testing of potential treatments. There are numerous success stories of how it has benefited humans, for example; the use of the mouse model for the development of rabies vaccine and pig models for skin graft in burns research. On the other hand, animals have also benefited from research, for example; dog heart valves and hip replacements and breeding programs for endangered species. The Lacrimal drainage system has not been an exception to this, with benefits of deeper understanding flowing both ways. (Paulsen et al., 2002; Maeda et al., 1999; Burling et al., 1991; Quantz and Stiles, 2019; Jugant et al., 2019). The search for an appropriate animal model for lacrimal drainage disorders is far from over and customization for specific anatomical or physiological objectives may be the way forward (Paulsen et al., 2002; Frame and Burkat, 2009; Hirt et al., 2012; Rehorek et al., 2011). Understanding the unique lacrimal drainage system of different species helps in acquiring the evolutionary perspectives in greater detail. Similarly studying the lacrimal drainage disorders (LDD) of various species and their management provides deeper understanding in relation to humans. Vice-versa, comparisons would provide the veterinarians the advantage of possibly applying the human medical and surgical advances to the extent possible for the animal kingdom. This major review addresses lacrimal drainage disorders in selected and common animal species, modalities employed for their treatment, comparisons with humans and how animal and human research may be able to contribute more to each other.

2. Methods

A systematic Medline search was performed on PubMed using variable combinations of the terms 'lacrimal', 'lacrimal sac', 'nasolacrimal duct', 'animal', 'primate', 'dog', 'cat', 'rabbit', 'pig', 'cat-tle', 'calves', 'horse', 'sheep', 'mouse', 'rat', 'reptile', 'amphibian', 'snake', 'salamander', 'crocodile', 'tetrapod's', 'mammal', 'obstruction', 'epiphora', 'infection', 'dacryocystitis', 'anomaly', 'fistula', 'lavage', 'anatomy', 'excretory', 'pathogenesis', 'etiopathogenesis', 'causative'. There was no restriction on the date of publication. All articles published in English with specific reference to disorders of the lacrimal drainage in the animal kingdom were assessed for the analysis. Relevant cross references from these articles were also considered. Data captured include demographics, presentations, investigations, diagnoses and management modalities. Emphasis was also on anatomical differences, evolutionary perspectives and addressing the lacunae and potential directions for future research.

3. Results

3.1. Evolutionary perspectives

The evolutionary origin of the nasolacrimal duct (NLD) is a source of some debate, with origins being either the infraorbital sensory canal of Osteolipiformes or the hind nasal tube of Crossopterygii fish (Medvedeva, 1986). The NLD has been observed in most major tetrapod extant taxa (amphibian, reptile, bird and mammal) with substantial variation in presence within each of the taxa (Hillenius and Rehorek, 2005): it is absent in some salamanders (Siegel et al., 2018), all turtles (Hillenius and Rehorek, 2005) and in scattered mammals (Rehorek et al., 2010, 2018).

It has been proposed that, in ancestral tetrapods, the NLD connected the Harderian gland (an anterior orbital gland) to the vomeronasal organ (VNO: a chemosensory structure in the floor of the nasal cavity) (Hillenius and Rehorek, 2005). In both squamate reptiles (Rehorek et al., 2000) and Caecilians (Wake, 1985), the secretions of the orbital gland flow into the NLD and then pass down to the VNO (Fig. 1A). In snakes, these orbital gland secretions are believed to solubilize pheromones which are then transferred to the VNO via the NLD for subsequent actions (Huang et al., 2006).

In both avesuchians (birds and crocodylians) and mammals, this is not the case. In archosaurs, the NLD is shortened and fails to reach the anterior part of the nasal cavity (Hillenius and Rehorek, 2005) (Fig. 1B). As a result, there are two main adaptations of the lacrimal drainage apparatus. Firstly, the NLD in crocodylians is a more glandular in structure (Rehorek et al., 2005). This, in addition to the orbital gland secretions, may be part of the reflex secretions that pass through the NLD to the oral cavity to moisten and soften the bolus of food (Murube, 2005, 2009). Secondly, the Harderian gland takes on another, more immunological function (Hillenius and Rehorek, 2005). The antibody rich secretions of the Harderian gland are transferred to the upper respiratory tracts via the NLD (Hillenius and Rehorek, 2005; Burns, 1992). Hence the NLD, is an important part of the Avesuchian head-associated lymphatic system. This can in part be compared to the human lacrimal drainage-associated lymphoid tissues (LDALT) (Paulsen et al., 2000a; Ali et al., 2013).

In mammals, however, the NLD, when present, bypasses the VNO and end up closer to the narial region (Fig. 1C), an association which has been correlated with the absence of a septomaxillary bone, guiding the NLD to the VNO (Hillenius, 2000). Once again, the function of the associated Harderian gland appear to be modified (Hillenius and Rehorek, 2005). The NLD is absent or incompletely developed in scattered bat species, with no apparent correlation to relative VNO development (Rehorek et al., 2010). However, there are two recent fetal studies which question this type of observation. Firstly, the adult configuration of a shortened NLD in Tarsiers and some anthropoid primates is different to the fetal condition. In this case, the NLD consists of a caudal boney aspect and rostral membranous portion, both of which are present in fetal life. However,

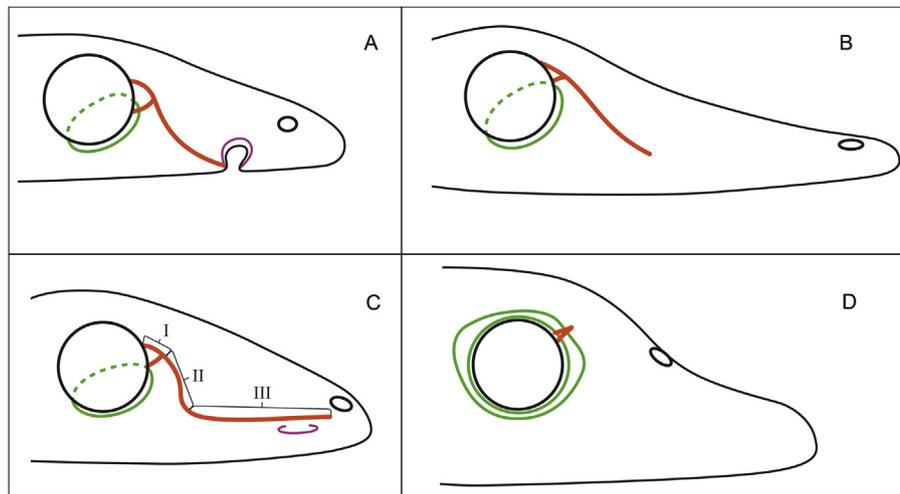


Fig. 1. Simple schematics showing the associations of the lacrimal drainage apparatus in representative tetrapod species, specifically Lizards (A), Avesuchian (B), typical mammal (C) and dolphin fetus (D). Key: Harderian gland (green), NLD (red) and VNO (purple), I-palpebral part, II-osseous part, and III- membranous part. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

at the perinatal stage, this membranous portion “unzips”, leaving the bony portion of the NLD to open caudally in the nasal capsule (Rossie and Smith, 2007). Secondly, a recent description of a transient NLD in dolphin fetuses (Fig. 1D), in whom adults NLD has been implied but never identified (Rehorek et al., 2018). Thus, it appears that fetal studies are needed in order to fully understand the true distribution of the NLD in the tetrapod lineages.

3.2. Dog

The lacrimal drainage system (LDS) of dogs begins with two, oval to elliptical puncta situated on the tarsal conjunctiva, 0.5–1 cm from the medial palpebral fissure (Hirt et al., 2012; Evans and de Lahunta, 2013; Barnett et al., 2002; Gelatt et al., 1972). The puncta are not very prominent and at a greater distance from the lid margins, unlike those of the humans. The upper and the lower canaliculi continue subconjunctivally in a bow shaped fashion for 5–7 mm before ending into the lacrimal sac (LS), situated in the bony lacrimal fossa (Evans and de Lahunta, 2013; Gelatt et al., 1972). The lower canaliculus enters the LS at an angle of 45–60 degrees (Gelatt et al., 1972). The LS is approximately 3–10 mm in size (Hirt et al., 2012; Gelatt et al., 1972). The NLD, unlike humans, is very long (10 cm) and depends on the cephalic confirmation and varies between dolichocephalic and brachycephalic breeds. It arises as a continuation of the LS and runs into a proximal bony osseous canal which ends underneath the first third portion of the maxilloturbinate. The rostral portion continues its course submucosally and follows the root of the maxilloturbinate (Hirt et al., 2012). At the level of the superior carnassial tooth, numerous accessory openings from the NLD to the nasal cavity are noted, whose functions are believed to moisten the large nasal surface area (Hirt et al., 2012). It opens in the ventral nasal meatus of the nasal cavity, 5 mm ventral to the root of the lower turbinate (Hirt et al., 2012; Gelatt et al., 1972). The histology and ultrastructure of the dog LDS is similar to humans in many ways including epithelial structure, microvilli, kinocilia, sub-epithelial cavernous bodies and mucosal associated lymphoid tissues (Hirt et al., 2012). Hence, the dog is also proposed as a good animal model not only for dry eye disease but also for the LDS (Hirt et al., 2012; Barabino and Dana, 2004).

Clinical presentations of LDD in dogs include chronic epiphora, discharge, matting of hair in the tear-trough region (Fig. 2), discoloration of the hair secondary to tear lactoferrin (Fig. 2), swelling over the lacrimal sac fossa and regurgitation of discharge on com-



Fig. 2. Clinical external image of the left eye of a brachycephalic dog (Shih Tzu). Note the gross epiphora, matting of hair in the tear trough and focal brownish discoloration of the hair. Also note the large pre-corneal tear drop.



Fig. 3. Clinical external image of a right eye of a dolichocephalic dog. Note the irrigation of lacrimal drainage demonstrates a complete regurgitation of the fluorescein fluid from the opposite punctum suggesting a nasolacrimal duct obstruction.

pression over the lacrimal fossa. Clinical examination includes visualization of the puncta, fluorescein dye disappearance, NLD transit time, Irrigation of the NLD (Fig. 3), and dacryocystorhinography and computed tomographic-dacryocystography (CT-DCG) (Gelatt et al., 1972; Yakely and Alexander, 1971; Binder and Herring, 2010; Rached et al., 2011). The NLD transit time in dog varies with the breed and is useful using fluorescein drops rather than fluorescein strip. However, it has not been found to be a very reliable clinical test in brachycephalic breeds like the Shih Tzu,

Pug and Pekingese (Binder and Herring, 2010) (Fig. 2). Due to the anatomical factors, the brachycephalic dogs and cats are more susceptible to LDD as compared to the dolichocephalic breeds (Gelatt et al., 1972; Binder and Herring, 2010; Grahn and Sandmeyer, 2007; White et al., 1984; Yi et al., 2006). CT-DCG with its 3D reconstruction is superior to the routine dacryocystorhinography and reliably depicts not only the bony NLD disorders but also the surrounding soft tissues despite limited orbital contrast imaging (Rached et al., 2011).

Numerous LDD are known in dogs and include punctal agenesis, punctal stenosis, foreign bodies, primary and secondary nasolacrimal duct obstruction (NLDO), cystic dilatation of NLD, dacryocystitis, lacrimal trauma, dacryolithiasis, NLD tumors and secondary epiphora from prolapse or cyst of the third eyelid (Quantz and Stiles, 2019; Barnett et al., 2002; Gelatt et al., 1972; Grahn and Sandmeyer, 2007; White et al., 1984; Yi et al., 2006; Stanley and Blogg, 1991; Grahn and Mason, 1995; Barbe et al., 2017; White and Brennan, 2018; Nykamp et al., 2004; Pope and Champagne, 2001; Lussier and Carrier, 2004; Voelter-Ratson et al., 2015; Malho et al., 2013; Lavach et al., 1984; Liang et al., 1988).

Punctal stenosis is not widely reported but has been described mostly in Siberian husky dogs and German Shepherds (Quantz and Stiles, 2019; Stanley and Blogg, 1991). The common underlying cause is prolonged topical medications and neomycin-polymyxin B-dexamethasone combination is the usual incriminating agent (Quantz and Stiles, 2019). Epiphora may not be a major presenting symptom and the diagnosis can be at times accidental. Slit lamp biomicroscopy demonstrates a narrow punctum with fibrosis in the vicinity and probing or attempt at NLD flush may not be possible because of associated canalicular stenosis (Quantz and Stiles, 2019). It is likely that acquired punctal stenosis in dogs demonstrate a similar clinical spectrum like those in humans and this belief is strengthened by the similar histopathological changes noted in dogs and humans (Quantz and Stiles, 2019; Ali et al., 2015). The treatment in dogs with discontinuation of the inciting drug was possible, however the stenosis was persistent (Quantz and Stiles, 2019). Investigations like retrograde dacryocystorhinography to localize the distal extent of the stenosis and surgical options like conjunctivorhinostomy and conjunctivobuccostomy have been proposed but not performed (Quantz and Stiles, 2019). Punctoplasty like in humans has not been tried so far but it would make sense to attempt either a punctoplasty or a good punctal dilatation with stents like in humans (Singh et al., 2018). The use of stents in this condition should be possible since punctal plugs of various diameters have been used in the management of canine keratoconjunctivitis sicca (Gelatt et al., 2006; Williams, 2002).

Recurrent dacryocystitis and NLDO followed by NLD cyst are not uncommon among dogs (Yakely and Alexander, 1971; White et al., 1984; Lussier and Carrier, 2004). The initial obstruction of the NLD can be secondary to intraluminal factors like debris accumulation and inflammation, and foreign bodies. Extra-luminal compressions can also cause cystic dilatation of the NLD and include trauma or neoplasia. The initial diagnosis of NLDO is based on lacrimal duct irrigation, which shows obstruction. Occasionally a forceful irrigation clears the debris, only to recur (Lussier and Carrier, 2004). Other clinical clues to the presence of NLD cyst includes swelling of the medial canthus or a medial canthal subconjunctival cyst (Grahn and Mason, 1995; Lussier and Carrier, 2004; Martin et al., 1987). This should be differentiated from the more proximal cystic dilatation of the canaliculi called canaliculops, which presents similar to that in humans (Gerding, 1991; Ramyil et al., 2018). Another differential diagnosis is orbital cysts in the vicinity compressing the NLD (Featherstone and Llabres-Diaz, 2003; Zimmerman et al., 2019). Contrast DCG or CT-DCG is critical in establishing the diagnosis. Cystic NLD dilatation secondary to NLD obstruction are usually acquired but juvenile occurrence of them in Dachshund and

Labrador has led to a speculation that it could also represent a similar clinical spectrum like that of congenital dacryoceles in humans (White et al., 1984; Lussier and Carrier, 2004; Singh and Ali, 2018). Although a conjunctivorhinostomy can be performed, most cases have been successful with either marsupialization or partial excision of the NLD cyst and establishing a wide communication with the nasal cavity (White et al., 1984; Lussier and Carrier, 2004; van der Woerd et al., 1997). Endoscopic guidance has been reported to be helpful in this maneuver (White et al., 1984).

Dacryocystitis and NLDO following dental anomalies is not uncommon in dogs and cats (Gelatt et al., 1972; Nykamp et al., 2004; Ramsey et al., 1996). A 5-year old Border collie was reported with chronic dacryocystitis secondary to ectopic tooth (Voelter-Ratson et al., 2015), similar to the one presented in humans, although the anatomical relationship between the NLD and teeth is not so intricate in humans (Alexandrakis et al., 2000). There are also reports of NLDO secondary to tooth abscess, obstructed carnassial tooth and osteomyelitis of the maxilla. These cases resolved following conservative systemic treatment with or without tooth extraction (Gelatt et al., 1972; Nykamp et al., 2004; Voelter-Ratson et al., 2015).

NLDO and chronic dacryocystitis in dogs which do not resolve with conservative measures are usually treated with conjunctivorhinostomy or conjunctivobuccostomy or conjunctivomaxillo-sinusotomy, whereby a new lacrimal bypass is performed either directly into the nasal cavity or maxillary sinus or the oral cavity (Lavach et al., 1984; Liang et al., 1988; Long, 1975; Covitz et al., 1977; Seo et al., 1995; Giuliano et al., 2006). A polyethylene intubation for a few weeks is used as an adjunctive modality during the surgical procedures. These techniques have also been used in instances of punctal and canalicular agenesis (Long, 1975). The outcomes reported are mostly good, although complications include stent loss or migration, corneal ulceration, mucosal hypertrophy and closure of the fistula (Long, 1975; Covitz et al., 1977; Seo et al., 1995; Giuliano et al., 2006; Scotti et al., 2007). Nasolacrimal duct catheterization has also been used as an alternative modality of management in chronic dacryocystitis (Severin, 1972; Murphy et al., 1977). The advent of advanced endoscopic and radiological techniques has led to canines being treated with dacryoendoscopy and fluoroscopy guided NLD catheterization for NLDO secondary to a wide range of etiologies (Strom et al., 2018). The stents used were 3.5 French red-rubber urethral catheters or two French urinary pigtail polyurethane catheter. All cases except few with severe degrees of fibrosis or granulation tissues could be treated. Clinical improvement was noted in at least 60% of the treated cases (Strom et al., 2018). Other than these, successful parotid duct transposition has been reported in an attempt to bypass the tears into the oral cavity (Scotti et al., 2007). However, this technique has not gained popularity because of the surgical complexities.

Foreign bodies in the LDS causing NLDO or dacryocystitis is uncommon in canines (Pope and Champagne, 2001; Van der Woerd et al., 1997; Strom et al., 2018; Singh et al., 2004). Plant material like finer wood pieces, grass or seeds have been found. Other than the routine clinical presentation for any LDD, epistaxis, hemorrhagic mucopurulent discharge, sneezing and discomfort could be the additional manifestations. Contrast dacryocystography reveals either filling defects in the LS or NLD or may even obscure their visualization in severe cases. Nasal endoscopy is very useful for direct identification as well as removal of the foreign bodies, although occasionally an intraosseous surgical approach may be needed to restore the LDS (Pope and Champagne, 2001; Singh et al., 2004). There is a single report of canine dacryolithiasis, isolated from a successfully excised inferior canalicular cyst (Malho et al., 2013). Ultrasonographic features showed a well delineated cyst with free-floating hyperechogenic intraluminal material with no

acoustic shadowing. The mineral analysis of this dacryolith showed it to be entirely composed of calcium carbonate (Malho et al., 2013).

Tumors of the NLD are rare in canines. The tumors may be primary or more commonly secondary due to invasion into the NLD (Gelatt et al., 1970). The most common location of NLD obstruction in these cases is soon after its exit from the osseous canal. Clinical presentations can be epiphora, epistaxis, oral bleeding, facial swelling or mass lesions on the gums. Contrast dacryocystorhinography is crucial for the diagnosis, delineation of the mass lesion and treatment planning. Squamous cell carcinomas, adenocarcinoma and fibrosarcoma have been reported (Gelatt et al., 1972; Nykamp et al., 2004; Gelatt et al., 1970). However, treatment details of the LDS tumors are not well known but are likely to follow the general principles of oncology.

3.3. Cat

The lacrimal drainage system (LDS) in cats begins with a superior and inferior punctum, approximately 0.7 mm in diameter, located on the inner surfaces of the respective eyelid margins near the nasal palpebral commissure (Breit et al., 2003). The upper canaliculus was around 3 mm with a more vertical course and coursed directly into the lacrimal sac (LS) whereas the lower canaliculus was 4–5 mm, formed an arch and entered the LS at an angulation of 70–80° (Gelatt et al., 1972; Breit et al., 2003). The lacrimal sac was situated in the bony lacrimal fossa formed by the lacrimal bone. Unlike the dog, the LS in cats is better developed, spheroid or oval shaped and larger in size (5–8 mm) (Gelatt et al., 1972; Breit et al., 2003). An interesting finding is that the distal part of the LS is without any osseous protection and covered only with the nasal mucosa (Nöller et al., 2006). The nasolacrimal duct (NLD) originates from the LS at an angle of 80–90°, passes the lacrimal foramen at the level of the 2nd pre-maxillary tooth to enter the lacrimal canal (Breit et al., 2003). The NLD is 2.5–4 cm long and 0.7–1.5 mm in diameter (Gelatt et al., 1972). Unlike dogs, the diameter of NLD in cats is more uniform (Gelatt et al., 1972). The proximal third of the NLD is within the canal, formed medially by the maxilla and laterally by the basal lamina of the maxilloturbinate. Rostral to this turbinate the NLD is medially covered by the nasal mucosa and travels horizontally, parallel to the palate to open onto the ventrolateral floor of the nasal vestibule just below the alar fold (Breit et al., 2003). The cat NLD histology is quite different from that of humans. The epithelium is double layered with many goblet cells but intra-epithelial mucous glands, cavernous bodies and sub-epithelial sero-mucous glands are lacking (Paulsen et al., 2002).

Lacrimal drainage anomalies in cats diagnosed by the traditional investigations like fluorescein transit times, irrigation of lacrimal drainage and dacryocystorhinograms include obstruction, stenosis, ectasia, agenesis, dacryocystitis, nasolacrimal abscess, and secondary extra-luminal obstructions from masses in the vicinity (Gelatt et al., 1972; Binder and Herring, 2010; Grahn and Sandmeyer, 2007; Nöller et al., 2006; Rickards, 1973; Zemljic et al., 2011). Severe punctal stenosis and subsequent fibrosis have been reported in cats following chronic conjunctivitis and have been treated with conjunctivorhinostomy with varying degrees of success (Covitz et al., 1977; Anthony et al., 2010). This can be comparable to a conjunctivodacryocystorhinostomy performed in humans in cases of irreversible occlusion of the punctal opening or their loss following a trauma (Ali and Kaynak, 2018).

Anatomic and CT-dacryocystography (CT-DCG) studies of the LDS have identified brachycephalic cats like some of the Persian varieties to be more at risk of chronic epiphora (Breit et al., 2003; Schlueter et al., 2009). The NLD of brachycephalic cats show a right angle or an acute angled course (V shaped) and the distance from the root of the canine tooth to the lacrimal sac decreased to 1–2 mm as compared to 5 mm in domestic cats (European short-

hair) (Schlueter et al., 2009). In profound brachycephaly, the tip of the nose (with its NLD opening) is at a higher level than the inferior punctum (Schlueter et al., 2009). All these factors can hinder the drainage of tears through the LDS and predispose Persian cats to chronic epiphora and subsequent lacrimal disorders.

The lack of osseous protection of the distal portion of the lacrimal sac directly predisposes it to the influences of nasal mucosal inflammations and sinusitis and direct invasion of the mass lesions from the vicinity (Nöller et al., 2006; Keller, 2000). Epiphora is also the predominant symptom of chronic rhinosinusitis in cats (Keller, 2000; Schoenborn et al., 2003). In comparisons, the human bony NLD lies in the wall of maxillary sinus and the opening of the NLD is in the inferior meatus and hence susceptible to the nasal and paranasal disorders (Ali and Paulsen, 2019). However, whether this contributes to the commonly occurring primary acquired nasolacrimal duct obstructions (PANDO) is controversial in humans (Ali and Paulsen, 2019).

Iatrogenic nasolacrimal duct obstructions in cats following the canine tooth extraction is not very uncommon (Paiva et al., 2013). This is secondary to the close anatomical proximity of the NLD with radix of the maxillary canine. The problem can also be compounded in cats since their teeth are more brittle and liable to be fractured easily as compared to the dogs. Clinical presentations include epiphora, discharge and dacryocystitis. Chronic epiphora in cats can also present as chromodacryorrhea, where secondary to proteins like lactoferrin in tears, the hair around the eyes shows rust-stains. Periorbital dermatitis can also result in secondary irritation and bacterial infections (Ramsey et al., 1996). Two cases reported iatrogenic NLDO in domestic shorthair cats (DSH) (Anthony et al., 2010; Paiva et al., 2013). One presented following a canine tooth extraction and was treated conservatively with NLD saline irrigation and a systemic anti-inflammatory agent (Paiva et al., 2013). The other case had NLDO following a canine tooth fracture and subsequent root abscess, which was successfully managed by tooth extraction, abscess drainage and medical management (Anthony et al., 2010). Hence, epiphora following tooth extraction in cats should arouse the suspicion of an iatrogenic NLDO. In comparison, although the anatomy is not so intricate in humans, there have been reports of NLDO in pediatric and adult age groups secondary to location of the canine tooth bud, impacted canines or ectopic eruption of teeth (Alexandrakis et al., 2000; Giordano et al., 2014; Fayet et al., 2019). Idiopathic or recalcitrant dacryocystitis in Persian, Siamese and in DSH cats have been treated with conjunctivorhinostomy with polyethylene intubation (Covitz et al., 1977). The stent is usually retained for up to four months. Although a good success has been reported, the common complications include stent loss, stent-induced granulomas and corneal ulcers (Covitz et al., 1977).

Rare causes of NLDO in cats include mass lesions from the nose and sinuses compressing the NLD or invading it to cause a fistula, secondary to the wall erosion (Gelatt et al., 1972; Madewell et al., 1976). An 8-year-old DSH cat was diagnosed with squamous cell carcinoma of the right upper gum compressing the middle third of NLD, whereby the tumor was treated by radiotherapy rather than by surgery (Gelatt et al., 1972).

3.4. Horse

The LDS in horses begins as superior and inferior punctum on the inner surface of palpebral conjunctiva, adjacent to pigmented border of the eyelids (Castro, 2004; Latimer et al., 1984). The superior and inferior canaliculi traverse a short distance (4–5 mm), join and end in the lacrimal sac (LS). The sac is well developed and located in the bony lacrimal fossa formed by the lacrimal bone. As with many animals, the nasolacrimal duct is the major structure of LDS and is approximately 29–33 cm long, 2–3 mm in diameter and arguably has three distinct anatomical portions (Spadari et al., 2011). The

proximal portion of the NLD arises from the lacrimal sac and traverses through the bony lacrimal foramen in the maxilla (Latimer et al., 1984). Following its exit from the lacrimal foramen, it runs forward embedded in the medial accessory cartilage, which causes its lumen to be comparatively flatter. Following its exit from the cartilage, it traverses ventrally until it opens into the nasolacrimal orifice at the mucocutaneous junction on the floor of the vestibule, 5–7 cm from the external nares. In mules', however, the opening is on the nasal septum (Castro, 2004; Spadari et al., 2011). Retrograde endoscopic examination of the NLD has provided clues to the luminal surfaces of NLD, however, features of the equine lacrimal sac and canaliculi are yet to be established (Spadari et al., 2011).

Epiphora in horses can be secondary to a host of eyelid and ocular conditions and these should be initially evaluated before the lacrimal system (Ollivier, 2004). Investigations to assess the LDS included fluorescein dye disappearance test, which in horses would take 5–10 minutes to show up at the nasolacrimal orifice (Castro, 2004). The nasolacrimal flushing is usually carried out in a retrograde manner by cannulating the NLD orifice by a Tomcat catheter or any appropriate polyethylene tubing and flushing 5–10 of saline and observing the fluid at the medial canthi (Castro, 2004). Alternatively, flushing can also be performed in an anterograde manner, as in humans, through the inferior punctum. Like humans, the specific site of obstruction can also be determined in horses by dacryocystorhinography, endoscopy and computed tomography or magnetic resonance imaging (Spadari et al., 2011; Moore, 1992; Carslake, 2009).

Numerous congenital anomalies of the LDS are known in horses and include punctal atresia or agenesis, congenital lacrimal fistula, NLD aplasia and dysgenesis of the distal nasolacrimal orifice (Mason, 1979; Gilger et al., 2010; Grahn et al., 1999; Theoret et al., 1997; Latimer and Wyman, 1984; Lundvall and Cater, 1971; Stoppini et al., 2014). Clinical presentation varies from epiphora, secondary bacterial blepharconjunctivitis to bacterial dacryocystitis secondary to malformations (Moore, 1992). A 2-year-old Morgan filly was reported to have bilateral anomalous openings (Gilger et al., 2010). The filly had congenital lacrimal fistula along with supernumerary distal NLD orifices, additionally confirmed by a 3D CT-DCG. Epiphora was successfully treated with a fistulectomy and intubation with a 5 French male silastic urinary catheter (Gilger et al., 2010). A 6-month-old Arabian filly was diagnosed with a congenital atresia of the left nasolacrimal duct (akin to congenital nasolacrimal duct obstruction [CNLDO] in humans) following clinical and radiological investigations (Grahn et al., 1999). Such anomaly is the most common congenital disorder in equine LDS and is believed to be either due to extension of surface ectoderm in the facial groove or a lack of canalization of distal NLD as in humans (Grahn et al., 1999; Theoret et al., 1997). The filly was successfully treated with a stellate incision over the distal most end of NLD. Although such incisions are the standard treatment, diode-laser photocoagulation has also been used for the same purpose (Stoppini et al., 2014). A 4-month-old Peruvian Paso filly with a left sided incomplete nasomaxillary dysplasia demonstrated medial canthal dystopia, absence of the dorsal punctum and canaliculus, NLD aplasia and absence of the distal NLD orifice (Theoret et al., 1997). This is akin to the complex syndromic CNLDO seen in human babies (Ali and Paulsen, 2017). The filly was treated with a conjunctivomaxillostomy with intubation, which failed twice and was successful on the third attempt (Theoret et al., 1997).

Acquired LDS anomalies in horses include nasolacrimal duct obstructions, foreign bodies, dacryocystitis, trauma, dacryolithiasis, extraluminal compressions by suture exostosis or cysts, spread of dental infections or sinusitis to LDS, and dacryohemorrhhea (Brink and Schumacher, 2016; Ramzan and Payne, 2005; Wilson and Levine, 1991; Barber, 2005; Dawson et al., 2016; Cassotis and Schiffman, 2006; Schumacher et al., 1992). Chronic epiphora and

mucopurulent discharge from the eye as well as the NLD orifice, and dacryocystitis are common presentations (Moore, 1992; Brink and Schumacher, 2016; Robinson et al., 2016). Although numerous fungal species have been isolated from healthy NLD of horses, they are at best opportunistic and most infections are bacterial (Brilhante et al., 2016). Adult presentation of CNLDO or acquired NLDO in horse has been successfully managed by canaliculostomy with polyethylene or Foley catheter intubation (Brink and Schumacher, 2016; Robinson et al., 2016). This bypass of the proximal lacrimal system into the maxillary sinus could be performed under sedation and has been reported to be effective in NLDO of varied etiologies (Brink and Schumacher, 2016). The long-term results of this procedure are also encouraging (Robinson et al., 2016).

Injuries to the head are common in horses since they tend to pull back and throw their head back suddenly when they perceive danger. This can be compounded by unsafe environments or during their transportation. Medial canthal lacerations can involve the puncta or the canaliculi and the principles of repair are similar to that in humans. The cut ends are sutured over a probe followed by a silicone or silastic intubation of the entire LDS, which is brought out from the NLD orifice and secured to the skin for several weeks (Barber, 2005). Facial fractures involving the maxilla and the lacrimal bones can lead to NLD trauma. Fractures that lead to NLD transection may not present with epiphora initially since the tears would drain into the wounds (Barber, 2005; Caron et al., 1986). Plain DCG or CT-DCG are useful investigations to locate the site of injury and also for surgical planning (Nykamp et al., 2004). Minor injuries can be treated with silicone or polyethylene NLD intubation, however severe injuries with permanent NLDO respond well to canaliculostomy with intubation (Brink and Schumacher, 2016; Wilson and Levine, 1991; Barber, 2005; Robinson et al., 2016; Caron et al., 1986; Cruz et al., 1997). A 10-month-old quarter horse stallion who underwent a facial fracture reduction with plates and screws later presented with epiphora secondary to obliterated common nasolacrimal canal (McIlroy et al., 2001). Radiographic analysis showed the periosteal and fibrotic reaction of the compression fracture to occlude the nasolacrimal canal. The patient was successfully treated with removal of the plates and screws and a canaliculorhinostomy (McIlroy et al., 2001). In cases of trauma it is important to cross-tie the horse for a few days post-operatively to prevent repeated trauma to the wounds and prevent stent loss.

Dacryolithiasis in horses presents as mucopurulent ocular discharge and foul-smelling nasal discharge and can be mistaken on radiography as a mass lesion (Cassotis and Schiffman, 2006). A distal NLD dacryolith was successfully removed and mineralogic analysis showed it to be predominantly composed of carbonate hydroxyapatite and halite (Cassotis and Schiffman, 2006). However, no nidus could be found. This is in contrast to human LDS, where the lacrimal sac and NLD concretions are predominantly made up of mucopeptides and blood components most likely act as a nidus (Ali et al., 2018).

3.5. Rabbit

The LDS in rabbits starts from a single punctum, located on the tarsal conjunctiva, at the rostromedial aspect of the lower eyelid, near the medial canthus (Fig. 4) (Burling et al., 1991; Brown, 2006). The punctum continues as a short canaliculus of 4–5 mm and ends in a short, dilated lacrimal sac. The NLD begins from the LS and has two straight segments; the first is the bony portion within the lacrimal and maxillary bone, which traverses up to the ventral meatus and the second distal portion which runs parallel to the palate, continuing through the inferior meatus and opens into the lateral aspect of the nares (Rehorek et al., 2011; Brown, 2006). The rabbit lacrimal epithelium is double layered with subepithelial cavernous bodies. However, unlike humans, they do

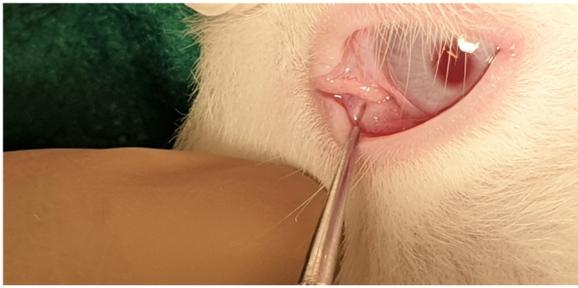


Fig. 4. Clinical external image of the left eye of a New Zealand white rabbit. Note the single inferior punctum away from the lid margin.

not have prominent goblet cells, intraepithelial mucous glands and subepithelial seromucous glands (Paulsen et al., 2002). The LS of the rabbits also has a distinct glycoconjugates distribution (Maeda et al., 1999).

NLDO is not uncommon in rabbits and unlike the horses, should be the first differential diagnosis for an epiphora presentation (Brown, 2006). The obstruction can occur because of the NLD constriction at two locations; at its entry into the bony foramen and at the base of the maxillary incisor (Brown, 2006). The etiology is believed to be *Pasteurella* infections, which may be primary or secondary to the inflammation and retention of lacrimal fluid in the LDS (Brown, 2006). Some authors presume the NLDO to be secondary to lipid droplets (Marini et al., 1996). Secondary NLDO can also occur due to the elongated roots of maxillary incisors or dental infections. The clinical presentation is usually that of chronic epiphora, discharge (important not to misjudge the milky secretions of the irritated third eyelid as discharge) and matting of the periorcular fur. Contrast radiography of the NLD with an iodinated dye can help in the diagnosis. Saline NLD flushing is a common procedure performed to remove the debris and relieve the NLD obstruction (Brown, 2006; Pilny, 2012; Graham, 2006). It is preferable to cannulate the lacrimal canaliculus with a catheter followed by gentle and intermittent flushing till the obstruction is relieved. Topical antibiotics and anti-inflammatory agents can be used. This can be performed over multiple sittings (Brown, 2006; Pilny, 2012; Graham, 2006). Potential complication of a poorly performed NLD flushing include lacrimal trauma, corneal injury and false passage creation (Brown, 2006).

Dacryocystitis, though not widely reported, is not a very uncommon ophthalmic disorder in rabbits. Two larger studies have shown dacryocystitis to comprise 2–73% of the ophthalmic diseases identified (Burling et al., 1991; Jeong et al., 2005). Malocclusion, rhinitis, pre-existing ocular infections or decreased immune status could all contribute to dacryocystitis. Diagnosis can be made based on clinical symptoms, secondary conjunctivitis or keratitis, LS swelling beneath the medial canthus, regurgitation on compression of the LS, NLD flushing and dacryocystography. A focused study on 28 rabbits with dacryocystitis revealed that the presentation was usually unilateral (89%), malocclusion was the common underlying factor (50%) and the mean duration of therapy was 5.8 weeks. In 35% of patients in this series, no underlying cause could be found as has also been reported earlier (Marini et al., 1996; Florin et al., 2009). This may be similar to primary acquired nasolacrimal duct obstruction in humans. Rabbits with dacryocystitis were treated with both topical and systemic antibiotics and anti-inflammatory agents and NLD flushing. However, only 43% (n = 12) showed complete recovery and 28% (n = 8) were euthanized. The authors of this review did not come across a documented report of a surgical LDS bypass in rabbits. Given the clinical scenario and outcomes of dacryocystitis, there is a need to explore the nuances of these procedures to better manage this condition.

Rabbits have been well studied as animal models for lacrimal disorders and their interventions and include experimental dacryocystitis, NLDO, NLD stents, retrograde catheterization techniques, balloon dacryoplasty procedures and NLD fluid resorption studies (Paulsen et al., 2002; Maeda et al., 1999; Cardoso et al., 2013; Ye et al., 2015; Hou et al., 2017; Goldstein et al., 2006; Wilhelm et al., 2006). Interestingly, it was rabbits in which it could be shown that components of tear fluid are reabsorbed in the nasolacrimal passage suggesting a feedback mechanism for tear fluid production (Paulsen et al., 2002).

3.6. Cattle

The LDS of cattle is like most mammals, having a superior and inferior punctum, canaliculus, LS, NLD and the NLD orifice which opens in the rostral nasal cavity. Clinical and radiological investigations of the LDS are similar to those of the horses. Disorders described in cows and bulls include congenital lacrimal fistula, supernumerary puncta and canaliculi, punctal and canalicular agenesis and proximal nasolacrimal duct anomalies (Jugant et al., 2019; Heider et al., 1975; Braun et al., 2012, 2014; McLaughlin et al., 1985; van der Woerd et al., 1996). Congenital lacrimal fistula is by far the most common congenital lacrimal anomaly and is seen in Brown Swiss and Holstein breeds (Jugant et al., 2019; Braun et al., 2012, 2014). It is hereditary and 20.4% of offspring were affected (Braun et al., 2014). In a large series 55% (30/54) were bilateral cases (Braun et al., 2014). Clinical presentations include epiphora, discharge, matting of the hair in the vicinity, pigmentation of the opening, inflammation of the fistulous tract and peri-fistula dermatitis. Alopecia around the fistula can allow for its easy detection. The location of the fistulae in most cases was at 3–4 o'clock position on the right side and 7–9 o'clock position on the left side (Braun et al., 2014). Fistulae ranged from 1 to 10 mm in height and 1 to 12 mm in length (Braun et al., 2014). The shape of the opening was mostly circular followed by oval and slit-like. Diagnosis is by anterograde and retrograde irrigation of the lacrimal system using an intramammary tube or similar appropriate ones (Jugant et al., 2019; Heider et al., 1975; Braun et al., 2012). Contrast dacryocystography or CT-DCG help in localization of the fistula (Jugant et al., 2019; Heider et al., 1975). Treatment consists of first intubating the NLD with the help of 6-French male silastic urinary catheter, to prevent its injury during the procedure (Jugant et al., 2019). Following intubation, fistulectomy is performed through an elliptical cutaneous incision. The intubation is usually retained for 2–3 weeks. The reported outcomes are successful (Jugant et al., 2019). A proximal nasolacrimal duct anomaly in a bull failed to respond to NLD intubation and was subsequently treated with a conjunctivorhinostomy into the ventral nasal meatus with prolonged intubation (Wilkie and Rings, 1990).

3.7. Camel and camelids

The one-humped camel does not show a punctum, however, two blind ducts, dorsal and ventral, approximately 1 cm long, 5 mm away from the medial canthus and 1 mm from the lid margins have been noted (Abdalla et al., 1970; Sadegh et al., 2007). The lacrimal sac is funnel shaped situated in a bony lacrimal fossa and continues as a 20 cm long and 3–4 mm wide nasolacrimal duct. The NLD opens as a mucosal opening in the anterior aspect of nasal process at the level of palatine fissure (Abdalla et al., 1970; Sadegh et al., 2007). The authors presume that absence of puncta is the reason for epiphora in one hump camels. However, no detailed studies of the blind ducts are available. The presence of well-developed lacrimal sac and NLD may point towards a possible functioning of the system. On the other hand, absence of puncta and blind ducts may point towards a possible and ongoing evolutionary loss of the LDS.

The LDS is however well developed in other members of the Camelid family like the llamas (Sapienza et al., 1992) and alpacas (Sandmeyer et al., 2011; Mangan et al., 2008). There are reports of bilateral absence of superior punctum in a 2-week-old female cria (Sandmeyer et al., 2011). Congenital nasolacrimal duct obstructions have been reported in young alpacas (Sandmeyer et al., 2011; Mangan et al., 2008). Clinical features include chronic epiphora, discharge and crusting and matting of hair below the eye. Dacryocystorhinography confirms the diagnosis. The lacrimal system in these cases is first cannulated through the inferior canaliculus using a 3.5 French x31 cm polyethylene infant feeding tube (Sandmeyer et al., 2011). The tube is passed till the inferior obstruction, just like the probing procedure in humans. An incision is then made in the nasal mucosa at the distal end of the catheter, which is pulled a little out and secured on the skin for six weeks, similar to the intubation procedure in humans. Good response has been reported with this technique (Sandmeyer et al., 2011). A 2-month old alpaca with bilateral congenital nasolacrimal duct obstruction was successfully treated with conjunctivomaxillostomy on one side and conjunctivorhinostomy on the contralateral side (Mangan et al., 2008).

3.8. Other animals

There are quite a few animals where the lacrimal drainage systems disorders and their management strategies have not been well studied.

3.8.1. Snakes

The LDS in snakes begins as a single punctum in the ventronasal subspectacular space and continues as a tortuous lacrimal duct and opens into the oral cavity in close association with vomeronasal organ (VNO) (Souza et al., 2015; Kaczmarek et al., 2017). An adult male blood python presented with subspectacular swelling secondary to the lacrimal duct obstruction, which was confirmed by a fluorescein lavage (Millichamp et al., 1986). The patient was successfully treated with a conjunctivoralostomy, which allowed drainage of retained secretions from the subspectacular space to the oral cavity (Millichamp et al., 1986).

3.8.2. Mice and rats

Mice and rats have well developed LDS like other mammals but histologically are different. The epithelium of the NLD is a stratified squamous epithelium with goblet cells and intra-epithelial mucous glands but without cavernous bodies and sub-epithelial seromucous glands (Paulsen et al., 2000b; Nakano, 1990). Rats and mice have been commonly used as lacrimal drainage models for studying embryology, anatomy, NLD resorption and LDALT (Paulsen et al., 2002, 2000b; Rehorek et al., 2015; Lotz et al., 2006; Lohrberg et al., 2018). However, the same is not true when it comes to the diseases of their LDS and treatment strategies. There is a single report of spontaneous squamous cell carcinomas arising from the NLD of rats secondary to chronic inflammation and additionally contributed by malocclusion (Schoevers et al., 1994).

3.8.3. Pigs

The LDS in pigs consists of upper and lower puncta and canaliculi which open separately into a lacrimal sac, which further leads to the NLD, the most prominent of the lacrimal ducts (Paulsen et al., 2002; Kyllar et al., 2016). Like in humans, the epithelium of the NLD in pigs was double-layered with surrounding cavernous body and sub-epithelial sero-mucous glands. However, unlike in humans, the goblet cells and the intraepithelial mucous glands were absent (Paulsen et al., 2002). The literature search did not reveal much about LDS and its disorders in pigs. Although it is an established model for craniofacial and orbital research, its utility as an animal model for LDS is yet to be ascertained (Kyllar et al., 2016; Lagalla

et al., 2000; Stembirek et al., 2012). The pig canaliculus, however, has certain well-defined mechanical properties and this could be utilized to study the canalicular physiology (Zhu et al., 2007).

3.8.4. Sheep and goat

The LDS of sheep and goats are similar (Gilanpour, 1979; Shadkhast et al., 2008; Moore and Whitley, 1984). The lacrimal puncta were slit-like, a bit large (1.5 mm), and present on the tarsal conjunctiva, 1 mm from the lid margin and 3 mm from the medial canthus. The canaliculi are approximately 7 mm and end in the 6 × 5 mm lacrimal sac situated in the bony lacrimal fossa. The NLD is 47–50 mm long and traverses first through the bony NLD in the maxilla and subsequently opens as a 1.5–2 mm opening in the lateral wall of the nose, 15 mm from the dorsal angle of the nostril (Gilanpour, 1979). It is interesting that the heads of these animals have been explored for training in endoscopic dacryocystorhinostomy, but did not gain prominence because of the lack of a demonstrable lacrimal sac (LS) (Gardiner et al., 1996; Mladina et al., 2011). The presence and structure of LS is controversial but is still worth a detailed exploration as an animal model for lacrimal surgeries.

3.8.5. Apes

Apes have an LDS that anatomically is similar to that of humans with similar histology. However, there is a difference of opinion on the goblet cells. The earliest primates had distinct orientation and angulation of the bony NLD with physiological functions inter-related with the VNO, which changed with evolution. Apes as an animal model for LDS has logistic limitations. It is strange that not much literature could be found on the disorders of lacrimal drainage in apes, but gross anatomical and histological similarities suggest potential similarities in pathologies as well.

4. Conclusions

The lacrimal drainage system has evolved considerably, adapting to the needs of the species. Uniform reporting of disease terminologies is needed. Diagnostic challenges in clinical examination require the development of customized lacrimal instruments. Multiple animals can be used as a model for human LDS based on the research objectives, needs and logistical factors. It is essential to understand in depth the lacrimal drainage disorders of animals commonly seen in veterinary practice, so that animal and human lacrimal sciences contribute more meaningfully to each other.

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CRediT authorship contribution statement

Mohammad Javed Ali: Conceptualization, Data curation, Formal analysis, Writing - original draft. **Susan J. Rehorek:** Formal analysis, Supervision, Writing - review & editing. **Friedrich Paulsen:** Supervision, Writing - review & editing.

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