Distichiasis: An update on etiology, treatment and outcomes

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Distichiasis, an extra row of eyelashes emerging from meibomian gland orifices, occurs due to the metaplastic transition of sebaceous glands into the pilosebaceous unit. It can present congenitally, such as in lymphedema distichiasis syndrome, or secondary to acquired conditions, such as cicatrizing conjunctivitis, trachoma. This review summarizes the etiology of distichiasis, its presentation, the evolution of various surgical techniques, and their outcomes in human and animal eyes. The published literature has focused on the different treatment modalities and their outcomes; the etiopathogenesis of this condition remains elusive. Truncating mutations (missense, frameshift, and nonsense) in the Forkhead family gene FOXC2 are involved in the distichiasis–lymphedema syndrome. The treatment options are no different for congenital versus acquired distichiasis, with no specific available algorithms. Acquired distichiasis in cicatrizing ocular surface diseases is difficult to manage, and existing treatment options offer success rates of 50%–60%. The outcomes of electroepilation or direct cryotherapy are not as good as surgical excision of distichiasic lashes after splitting the anterior and posterior lamella under direct visualization. The marginal tarsoctomy with or without free tarsoconjunctival graft has shown good results in eyes with congenital and acquired distichiasis. The details of differences between normal and distichiasic lash, depth, or course of distichiasic eyelashes remain largely unknown. Studies exploring the distichiasic eyelash depth might improve the outcomes of blind procedures such as cryotherapy or radiofrequency-assisted epilation.

Key words: Congenital, cryotherapy, distichiasis, electroepilation, eyelash, Stevens-Johnson syndrome

Distichiasis (di = two, stichos = row) refers to an eyelash abnormality where eyelashes stem from meibomian gland orifices. Normal eyelashes are situated within the anterior lamella of the eyelid, arising from skin epidermis, and are comprised of pilosebaceous unit [Fig. 1]. Distichiasis should be carefully distinguished from trichiasis, which refers to misdirection of otherwise normally positioned eyelashes. Other lash disorders, such as tristrichiasis (three rows of eyelashes), tetrastichiasis (four rows of cilia), and drug-induced eyelash trichomegaly (increased eyelash length and curling), should not be confused with distichiasis. The distichiasic eyelashes grow from or adjacent to the sebaceous gland orifices and produce symptoms secondary to ocular surface rubbing. The eyelashes may be thick, thin, pigmented, or nonpigmented. It can be of two types: congenital and acquired. Although these eyelashes can be removed by simple epilation, electrolysis, radio ablation, cryotherapy, argon laser, or surgical excision, the need for repeated sessions of therapy for multiple recurrences remains a significant nuance. The exact mechanism behind recurrence and complications is less clearly understood despite the multiple surgical advancements made since the 19th century. This review summarizes the etiology of distichiasis, its presentation, and the evolution of various surgical techniques and their outcomes along with future research possibilities.

Methods

A thorough literature search for the articles published on human and animal distichiasis from 1960 to 2020 in English was performed in PubMed. The search used the terms “distichiasis,” “congenital distichiasis,” and “acquired distichiasis.” Of the 80 abstracts reviewed, 61 were included for the review, excluding the duplication/nonspecific/non-English/noncontributory material. A review of the references of relevant articles was also performed.

Distichiasis in Animal Population

Prevalence and etiology

In canines, the incidence of distichiasis is much higher (1:133) than in human beings (1:10000). There is no sex predilection noted in animals with distichiasis. However, female cocker spaniels are more likely to show distichiasis than males among canines. Distichiasis is uncommonly observed in horses, cats, and ferrets. In contrast to the distichiasis seen in humans, which can be acquired, distichiasis in animals is usually congenital. Its inheritance is presumed to be autosomal dominant; however, it has not been formally proven. The exact etiology of this condition is unknown. Histological study of 21 excised tarsoconjunctival strips bearing cilia from 20 canines showed some anatomic segments (hair follicle, hair bulb, or hair shaft) of hair follicles originating within the tarsus, in proximity or in direct connection with the tarsal glands. These glands were essentially normal, and the hair follicles with or without shafts passed in between the tarsal glands’ lobules or inside the excretory duct of the glands. This is in

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contrast to the findings observed in congenital distichiasis in human eyes, where meibomian glands are few or rudimentary.

Clinical presentation
Clinically, animals with distichiasis present with eye irritation, and they frequently rub their eyes on the carpet. Watering from the eyes is the second most common complaint. The severity of symptomatology depends on the number and size of cilia. Ocular examination reveals the extra eyelashes arising from meibomian gland openings. These can have variable lengths and have very fine tapering tips, which might require visualization under a magnifying lens. If they are nonpigmented, then a close observation is needed for their detection. Soft fine lashes do not cause any discomfort and can be an incidental finding. Lashes that contact the cornea or ocular surface present with symptoms of watering, redness, and discharge. In severe cases, they may also present with blepharospasm, reactive thickening of the bulbar conjunctiva, superficial punctate keratitis, or corneal ulceration, especially where the distichiasic lashes are long and the animal has protruding eyes. In few cases, corneal vascularization may also be present. One should be mindful of pseudo-distichiasis in animals as their mucocutaneous junction is relatively posteriorly placed, especially in canines.

Management and outcomes
Treatment is warranted when the distichiasic lashes cause clinical signs of irritation. Various methods such as electrolysis, cryotherapy, laser ablation, or surgical excision have been employed with an overall success rate of 69%–88%. The choice of technique depends on the location and extent of involvement. Manual epilation using round-tipped epilation forceps provides a short-term relief with almost invariably recurrence. Nonsurgical methods include electrolysis, cryotherapy, and transconjunctival thermal electrocautery. The use of blend electrolysis (2–3 mA for 15–30 s) in 78 canines showed recurrence in 65% of eyes, lid margin scarring in 33% of eyes, and depigmentation in 27% of eyes. Transconjunctival thermal electrocautery in 88 canine eyelids was successful in 69% of cases, with recurrence in 25% and emergence of new distichiasic eyelashes in 6% of eyelids. The average time taken for eyelashes to regrow after electrolysis varies from 11 to 192 days. Surgical techniques described include partial tarsal plate excision, wedge resection, and palpebral conjunctival resection. Excision of a 2–3-mm wide tarsocconjunctival plate 2 mm away from the lid margin produced better success rates than electrolysis. Although the recurrence of distichiasis was reported in 5.3% of eyes, 46% of eyes developed new distichiasic eyelashes at 5 weeks from the surgery date, which must have been recurrence but labeled as emergence of new distichiasic lashes. Eyelid reconstruction using oral mucosa grafts can be performed for recurrent distichiasis that has undergone multiple interventions.

Congenital Distichiasis

Etiology
Lymphedema–Distichiasis syndrome (LDS), first described in 1899, is an autosomal dominant single-gene disorder, with high penetrance and variable expressivity manifesting with distichiasis in 94%–100% of patients [Fig. 2]. Congenital distichiasis can occur as an isolated condition, part of a syndrome like Setliss syndrome, or isolated with dysmorphic features, absent lacrimal ducts, and limb abnormalities. Truncating mutations (missense, frameshift, and nonsense) in the Forkhead family gene FOXC2 located on chromosome 16q24.3 gene are involved in distichiasis–lymphedema syndrome. No link has been established between the type of mutation and clinical phenotype. Occasionally, there can be no truncating mutation in FOXC2 gene but duplicated region 5’ of FOXC2 or balanced translocation in 16q24 seen in LDS patients. Almost 75% of LDS-affected individuals have one parent with distichiasis; in the rest, it can be a de novo presentation. Genetic testing and counseling should be advised for patients with congenital distichiasis.

Clinical presentation
It can be asymptomatic in eyes with corneal hypoesthesia. In addition, if distichiasic eyelashes are lanugo-like, then many patients can be asymptomatic. The presenting complaints are watering, irritation, redness, and, sometimes, photophobia. Clinically, the eyelid margin shows distichiasic eyelashes emerging from meibomian gland openings, positive corneal fluorescein staining, and faint corneal scars due to repeated corneal abrasions. The presentation is usually bilateral, with few reports of unilateral involvement. It can affect one or all four eyelids, with the number of distichiasic eyelashes varying from 4 to 27. The secretions from meibomian gland openings cannot be expressed wherever cilia are present. However, there are no reported studies on the lipid layer content of tear film in these patients.

The most common association of LDS are leg swelling (80%; most often develops at puberty), varicose veins (50%), ptosis (31%), conjunctival edema, congenital entropion, congenital heart disease (7%), and cleft palate (4%) [Fig. 2]. The other reported systemic associations are renal anomalies, extradural cysts, scoliosis, neck webbing, uterine anomalies, strabismus, synophrys, and hydrops fetalis. Rarely, this syndrome can be fatal due to systemic associations. A prenatal ultrasound can help in early detection if limb edema and associated heart defects are present. Lymphoscintigraphy can help differentiate LDS from other causes of primary lymphedema.

Histology in congenital distichiasis
There are few histological studies available on congenital distichiasis. In LDS, the bulk of meibomian glands are absent with few partially formed glands. The tarsal tissue is normal. It represents an atavistic change where there is a failure
of meibomian gland differentiation. Alkatan et al.\textsuperscript{[37]} found numerous hair follicles accompanied by small sebaceous glands in three congenital distichiasis patients. They postulated that the differentiation occurred in a pilosebaceous unit rather than sebaceous glands alone. They also found fibrosis and inflammatory infiltrate around the cilia which was attributed to the previous electroepilation or surgical procedures.

**Acquired Distichiasis**

**Etiology**

The reported etiologies of acquired distichiasis are chemical injury, Stevens–Johnson syndrome, ocular cicatrical pemphigoid, trachoma, chronic rosacea, and blepharitis.\textsuperscript{[38]} The exact prevalence of distichiasis in specific ocular surface disorders is unknown. The underlying mechanism is metaplasia and dedifferentiation of the meibomian glands that become pilosebaceous units containing hair follicles. Long-standing inflammation in the conjunctiva/meibomian glands/tarsus is considered responsible for inducing the metaplastic transformation.\textsuperscript{[2]} Rarely, it can occur as a complication of permanent tarsorrhaphy, possibly due to trauma to the tarsus and meibomian glands.\textsuperscript{[39]} Distichiasis and entropion have also been reported after chemotherapy for metastatic breast cancer with pertuzumab, trastuzumab, and docetaxel.\textsuperscript{[40]} Docetaxel produces subconjunctival fibrosis and lid margin inflammation that results in eyelid changes.

**Presentation**

The typical complaints are irritation, watering, and redness in the eyes. It can manifest with symptoms such as pain, photophobia, corneal erosion or ulceration, and corneal scarring. Ocular examination shows stunted and nonpigmented eyelashes originating from the meibomian gland openings. They may be fine and require slit-lamp examination for identification. Sometimes, they are noticed when patients misdiagnosed with allergic conjunctivitis do not respond to the usual treatment.\textsuperscript{[41]}

![Figure 2](image1.png)

**Figure 2:** (a) A 5-year-old child presented with congenital ptosis and distichiasis. All four eyelids have eyelashes originating from meibomian gland openings (b and c; marked with an arrow). (d)–(f) A 45-year-old female with lymphedema distichiasis syndrome developed entropion in the upper eyelid after repeated electroepilation and cryotherapy, and everted upper eyelid shows scarred tarsal conjunctival tissue (e).

![Figure 3](image2.png)

**Figure 3:** Acquired distichiasis in an elderly female involving lateral half of upper eyelid (marked with an arrow) (a); mix of trichiasis and distichiasis secondary to chronic conjunctivitis (b). Left upper eyelid of 32-year-old Stevens–Johnson syndrome patient shows keratinized marginal conjunctiva with small distichiasis eyelashes (c).
**Treatment of congenital and acquired distichiasis**

There are no different algorithms available for treating congenital versus acquired distichiasis. The existing treatment options seem unsatisfactory and treatment is tailored for individual cases. The existing management options for distichiasis include nonsurgical modalities, such as electroepilation and cryotherapy, and surgical modalities, such as tarsorrhaphy excision and direct eyelash excision [Table 1]. When different lash ablation techniques (electroepilation, cryotherapy, and laser ablation) were compared in rabbit eyelids, electroepilation resulted in focal destruction of lash follicles with eyelash regrowth whereas cryotherapy produced near-total destruction of eyelashes and follicles.\(^ {42}\) Argon laser was found to be least destructive and showed good results. The different techniques and their outcomes in eyes with congenital or acquired distichiasis are discussed below.

**Radioablation**

Electrolysis using radiofrequency cautery is the treatment of choice for distichiasis with minimal lid margin involvement. Surgical electrocautery produces extensive lateral heat and damage, resulting in irreversible scarring of the lid, and hence not recommended. Radioablation involves applying radiofrequency current (3.8 MHz) to the hair follicle for a duration sufficient to produce bubbles on the lid margin. It is usually applied for 1–2 s.\(^ {21}\) After ablation, the lash should self-epilate or one should be able to pluck off eyelashes easily without any force. In many cases, multiple sessions of electroepilation are needed to achieve a symptom-free state.\(^ {43}\)

The radiofrequency needle can be applied to the root of eyelashes blindly or under direct visualization. When performed blindly, the needle is inserted via the skin for a varying depth of 2–3 mm [Fig. 4]. The success of this technique depends on the ability of waves to reach up to the dermal papilla. The maximum reported depth of normal eyelashes in the UK population is 2.4 mm in the upper eyelid and 1.4 mm in the lower eyelid.\(^ {44}\) However, the depth of distichiatic eyelashes has been reported to be at 2.5–4.5 mm.\(^ {44}\) It is worth exploring in future studies as to whether the electroepilation needle stays coaxial with the hair shaft and follicle. In addition, population-based studies regarding the depth of normal and distichiatic eyelashes would be useful. The outcomes of electroepilation alone for distichiatic eyelashes are not widely reported.

Alternatively, eyelashes have been removed using current under direct visualization of its root. The direct view of the eyelash root is achieved after splitting the anterior and posterior lamella. Eyelashes can then be excised using a No. 11 Bard–Parker blade or low-power Bovie monopolar needle cautery (Colorado Biomedical, Evergreen, Colo) causing microhyfrecation.\(^ {6,11}\) The use of this technique in 17 eyelids resulted in one recurrence-free year in 35.3% of eyelids and trichiasis in 47% of eyelids.\(^ {6}\) Using a similar technique, another study reported a success rate of 84.6% in 45 patients with trichiasis and acquired distichiasis. The direct excision after exposing the eyelash root does not require any tarsorrhaphic incision or excision, thus reducing the risk of developing entropion postoperatively.

**Argon laser ablation**

Argon laser ablation has been described mainly for trichiasis and is used very rarely for distichiasis. Laser settings of 300 mW, 0.2–0.5-s duration, and 50-micron spot size are used for trichiasis.\(^ {45}\) The depth of laser burn is approximately 2 mm, which can be a difficulty for distichiatic eyelashes that are far deeper than trichiaic eyelashes. Hence, argon laser ablation is not advisable for distichiatic eyelashes.

**Cryotherapy**

Cryotherapy ablates the eyelash root by destroying the bulb area with low temperatures. The incomplete removal of distichiatic

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**Table 1: Summary of published articles on the management outcomes of distichiasis**

| Study/year | Surgical Technique | Type (No. of eyelids) | Anatomical Success (%) | Recurrence | Rx of recurrence (no. of eyelids) | Outcomes of recurrence | Mean follow-up in months (range) |
|------------|-------------------|----------------------|------------------------|------------|-------------------------------|-----------------------|-----------------------------|
| Anderson et al.\(^ {10}\)/1981 | Lid-split cryotherapy and anterior lamellar recession | Acquired (13) | 54% | 46% | Cryotherapy/epilation | Resolved | 12-48 |
| Wolffey et al.\(^ {10}\)/1987 | Direct eyelash excision | Distichiasis (26) | 80% | 20% | Resurgery | Resolved | 24 |
| O’Donnell et al.\(^ {11}\)/1993 | Lid-split cryotherapy and posterior lamella advancement | Congenital distichiasis (15) | 20% 87% (if symptoms based) | 80% | Observation/resurgery | Unable to comment | 24 (12-108) |
| Vaughn et al.\(^ {11}\)/1997 | Lid-split and monopolar cautery or direct excision | Congenital (12) Acquired (5) | 35% | Trichiasis (47%), distichiasis (6%) 15.4% | Cryotherapy (4), electrolysis (4) Resurgery (1) | Resolved (100%) | 12 |
| Chi et al.\(^ {11}\)/2005 | Lid-split and monopolar cautery | Trichiasis & distichiasis (52) | 84.6% | - | - | - | - |
| McCracken et al.\(^ {12}\)/2006 | Eyelash trephination | Acquired (2) | 100% | - | - | - | - |
| Rozenberg et al.\(^ {13}\)/2018 | Marginal tarsectomy | Congenital (1) Acquired (16) | 100% | - | - | - | 31 (8-104) |
| Galindo-Ferreiro et al.\(^ {14}\)/2018 | Lid-split, marginal tarsectomy and tarsoconjunctival free graft | Congenital (6) | 100% | - | - | - | 9 |
eyelashes can occur as a result of inadequate freezing point temperature, duration, or freeze depth. One must be cautious of using the right temperature to achieve good results. Accurate measurement requires intraoperative use of a thermocouple. Using high-flow nitrous oxide, the average time to reach −20°C is 42 s in the first cycle and 48 s in the second cycle. Delaney et al. recommended the first freeze cycle’s duration to be 60 s, followed by a slow thaw and a second cycle of 45 s, which results in a success rate of 82%. A freezing duration of 45 s and a slow thaw for 4 min has also been advised if there is no access to a thermocouple. Cryoablation can be applied with or without lid margin splitting. If performed without lid margin split (as in few eyelashes), cryoprobe is applied toward the conjunctival side. Transconjunctival application results in depigmentation of few regular eyelashes in individuals with pigmented skin. The results of direct cryotherapy for patients with acquired distichiasis secondary to cicatrizizing ocular surface disorders are not encouraging as there are reports of increased surface inflammation following the procedure.

The more commonly used technique for cryoablation of distichiasis is after lid margin splitting. For lid margins with extensive distichiasis, the anterior and posterior lamella splitting is preferred, followed by direct cryoablation to the distichiasis eyelashes in a double freeze–thaw manner [Fig. 5]. After cryotherapy, anterior lamella is recessed 4 mm beyond the posterior lamellar margin. The reported success rate of this technique is 54%. The repositioning of anterior lamella can be done with or without posterior lamella advancement. The anterior lamella recession or posterior lamella advancement is performed to prevent the postoperative complication of entropion. O’Donnell and Collins advanced the posterior lamella by recessing the eyelid retractors. Their technique worked well in congenital distichiasis with symptom relief (87% success rate) noted in all except two patients that required resurgery. However, the anatomical assessment revealed recurrence in all except three patients following one sitting of the abovementioned procedure, achieving an anatomical success rate of 20%. The Collin cryoprobe (Keeler Ophthalmic Instruments), which was specifically designed for eyelid use and shows the temperature change as well, was used in their study. Some authors believe that surgical approach should be the first-line therapy rather than cryotherapy alone.

The reported complications of cryotherapy are subconjunctival hemorrhage, prolonged eyelid erythema and swelling (lasting 2–3 months), trichiasis (9%), over-advancement of tarsus (6%), lid margin keratinization (20%), and reduced tarsal thickness. In patients with cicatrizizing ocular surface disorders, almost 75% of patients experience some complication, such as xerosis following cryotherapy that affects the disease progression within these eyes. Ocular surface diseases
usually have associated conjunctival keratinization that can resolve or progress after cryotherapy. One study reported resolution in 66% of cases when the probe is applied through the involved conjunctiva but progressed in up to 21% of cases.\[5,49\]

**Surgical options**

Surgical management of distichiasis eyelashes revolves around splitting the anterior and posterior lamella and removing exposed eyelashes by simple excision, cryotherapy, or electrocautery. All these procedures are performed under an operating microscope or using high-magnification surgical loupes. The first surgical removal of distichiasis eyelashes dates back to 1880, wherein the two lamellas were separated and the tarsoconjunctival strip containing cilia was excised, leaving a bare marginal area.\[53\] Rozenberg et al.\[46\] used a similar technique in 2018 and reported a 100% success rate with no complications; however, the study did not provide a detailed description of the outcomes. In 1913, Begle modified this technique by covering the bare area with mucous membrane graft.\[51\] In 1962, Fox attempted to correct distichiasis in a single case by excising the 3-mm-wide conjunctival flap containing distichiasis eyelashes and pulling up the resected conjunctival edge to the anterior lamella.\[55\] Fox and Begle reported successful outcomes with their technique, though in a single case each without presenting the long-term results. The most significant disadvantage of resecting marginal tarsoconjunctival flap without grafting is entropion.

Galindo-Ferreiro et al.\[54\] used tarsoconjunctival graft (to avoid entropion) for replacing the excised tarsus in three patients with congenital distichiasis and reported 100% success rates [Fig. 6a and b]. Sheth et al.\[59\] added levator recession for tarsal advancement and used mucous membrane graft for replacing excised marginal tarsoconjunctival in a 7-year-old male with congenital distichiasis. The technique achieved satisfactory functional and cosmetic outcomes. White used a similar technique in one case of congenital distichiasis with a successful outcome but excised the tarsus (containing the root of eyelashes) 1 mm away from the lid margin and filled the defect with buccal mucosa.\[57\] The resected tarsus depth was up to two-thirds of its thickness. The abovementioned techniques have been used for congenital distichiasis and are challenging to use for acquired distichiasis, especially in cicatrizing ocular surface diseases. The excision of tarsal tissue or conjunctiva would further shorten the posterior lamella in cicatrical ocular diseases.

To avoid marginal issues and tarsal excision, a transconjunctival trapdoor technique was devised. In this technique, an incision is made 2 mm away from the lid margin and deepened till the anterior tarsal border, thereby exposing the cilia root and removing it under direct visualization.\[58\] Though this technique does not require grafting or marginal tarsal excision or cautery assistance, its outcomes and recurrence rates are not available. In elderly individuals with dermatochalasis, redundant skin at the eyelid crease can be removed for additional lift.\[59\] Eyelash trephination using Sisler ophthalmic microtrephine, which has a diameter of 0.81 mm, has been used for eyelash removal. Recurrences were noted in 38% of patients with trichiasis and acquired distichiasis.\[43\] The unknown course and depth of abnormal eyelashes could be the potential reason for failed cases. Direct excision of distichastic eyelashes by making a vertical incision along the length of aberrant lash has also been tried in 22 eyes with congenital distichiasis.\[30\] It was successful in 80% of cases but requires around 1 to 1.5 h of surgical time per eyelid. For acquired distichiasis with lid margin keratinization and cicatrical entropion, anterior lamellar recession with direct excision of the root of distichastic lashes can be performed [Fig. 6c and d].\[54\]

The bare tarsal area, lid margin, and shortened posterior lamella are covered with labial mucosal graft.

The complications of surgical correction of distichiasis are recurrence, trichiasis, altered lid margin morphology, and eyelid malposition such as frank entropion. The issue with the abovementioned techniques is incomplete documentation of the depth of tarsal excision. The usual description says that a 2-3-mm-wide tarsoconjunctival strip is removed but the vertical extent (depth) is not mentioned. Distichiasis eyelashes are far deeper than trichiasis eyelashes (maximum depth of 2 mm), though the exact depth of distichiasis eyelashes is unknown, especially in acquired cases. Even the course of distichastic eyelashes is not always vertical, and they can extend to varying depths horizontally and vertically, as shown by Wolfley et al.\[40\]

The development of imaging modalities such as high-frequency ultrasound that can image the eyelash roots can aid in complete removal of distichastic eyelashes with their roots.

**Conclusion**

The management of distichastic eyelashes is tailored on an individual basis and depends upon the extent of lid margin involvement and ocular surface disease. The frequent recurrences have made the management of distichiasis a challenging experience for both patient and surgeon. Eyelid splitting followed by direct excision or tarsoectomy or cryotherapy achieves good results, with recurrences noted in 15%–40%. Studies evaluating the treatment options prospectively along with serial documentation of magnified lid margin photographs would be helpful in identifying the factors responsible for distichiasis recurrences. Furthermore, studies exploring the exact depth and course of distichastic eyelashes would be useful for improving the success rates.

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**Conflicts of interest**

There are no conflicts of interest.

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