5

Acquired Etiologies of Lacrimal System Obstructions

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Acquired obstructions of the lacrimal excretory outflow system will produce the symptoms of epiphora, mucopurulent discharge, pain, dacryocystitis, and even cellulitis, prompting the patient to seek the ophthalmologist for evaluation and treatment. Impaired tear outflow may be functional, structural, or both. The causes may be primary – those resulting from inflammation of unknown causes that lead to occlusive fibrosis—or secondary, resulting from infections, inflammation, trauma, malignancies, toxicity, or mechanical causes. Secondary acquired dacryostenosis and obstruction may result from many causes, both common and obscure. Occasionally, the precise pathogenesis of nasolacrimal duct obstruction will, despite years of investigations, be elusive.

To properly evaluate and appropriately treat the patient, the ophthalmologist must have knowledge and comprehension of the lacrimal anatomy, the lacrimal apparatus, pathophysiology, ocular and nasal relationships, ophthalmic and systemic disease process, as well as the topical and systemic medications that can affect the nasolacrimal duct system. One must be able to assess if the cause is secondary to outflow anomalies, hypersecretion or reflex secretion, pseudoepiphora, eyelid malposition abnormalities, trichiasis, foreign bodies and conjunctival concretions, keratitis, tear film deficiencies or instability, dry eye syndromes, ocular surface abnormalities, irritation or tumors affecting the trigeminal nerve, allergy, medications, or environmental factors. Abnormalities of the lacrimal pump function can result from involutional changes, eyelid laxity, facial nerve paralysis, or floppy eyelid syndrome, all of which displace the punctum from the lacrimal lake. If the cause is secondary to obstruction of the nasolacrimal duct system, the ophthalmologist must be able to determine where the anomaly is and what the cause is, in order to provide the best treatment possible for the patient.

Tearing is a common complaint, and a complete workup is multifaceted and requires a detailed history as well as a comprehensive ophthalmic examination with special emphasis on the anterior segment, lacrimal system, and nasal cavity. The cause of tearing can be secon-

dary to hypersecretion, lacrimation, or impairment of drainage. The patient should be questioned regarding the following: unilateral versus bilateral vision; subjective symptoms of foreign body sensation, burning; constant versus intermittent problems; allergies; prior use of medications; prior probing; sinus disease and/or surgeries; prior trauma, midfacial trauma, nasal fractures; radiation treatment to the periocular or paranasal sinus area; ocular diseases; ocular or periocular surgeries; prior episodes of lacrimal sac inflammation or infection; discharge; clear, or bloody tears.

Inspection of the eyelids and lashes may reveal signs of blepharitis, concretion, cyst, molluscum contagiosum, chalazion, ectropion, entropion, trichiasis, lid laxity, lagophthalmos, poor blinking mechanism which may be secondary to seventh cranial nerve paralysis, poor lacrimal pump function, and overriding of the upper and lower lids. A notch on the lid margin secondary to trauma or surgery may allow tears to flow out of the tear pool onto the face. The punctum should be evaluated for size, stenosis or occlusion, its position, movement, and for possible obstruction by the conjunctiva, the plica semilunaris, an enlarged caruncle, conjunctivochalasis, or hyperplasia. A badly slit punctum or canaliculus may also be a source of chronic epiphora. Palpation with pressure over the lacrimal sac may produce a reflux of mucoid or mucopurulent material through the canalicular system and punctum if the common canaliculus and valve of Rosenmüller are patent.

Examination of the nose should be performed to rule out the possibility of intranasal tumors, allergic rhinitis, polyposis, or turbinate impaction or other possible obstructions of the distal end of the nasolacrimal duct.

Symptoms of epiphora can reflect excess tearing, or hypersecretion of tears, caused by the reflex arcs initiated by such processes as keratoconjunctivitis sicca, keratitis, allergies, or uveitis. In some patients, the clinical examination is unremarkable and the cause of epiphora remains unclear, a functional block.

Unilateral tearing is suggestive of a lacrimal outflow problem because of either obstruction or poor function of the tear pump caused by weakness of the orbicularis muscle, seventh cranial nerve palsy, or lower lid laxity. Also to be considered in unilateral tearing is the possibility of intracranial processes, such as an acoustic neuroma, which can compress the lacrimal innervation pathway in the brain and result in decreased tear production and unilateral dry eye symptoms and signs, including epiphora. Lymphoma, adenoid cystic carcinoma, or other tumors of the lacrimal gland can infiltrate the gland and/or its innervation, causing decreased tear production on one side, with epiphora. However, bilateral outflow abnormalities can occur and result in bilateral tearing.

Symptomatic tearing can result when a normal lacrimal drainage system is overwhelmed by hypersecretion, or when a drainage system is anatomically comprised and unable to handle normal tear production. Epiphora is determined by a balance between tear production

and tear drainage and not by the absolute function or dysfunction of either.

Nasolacrimal duct occlusion is more common in the middle-aged woman, is often of unknown etiology, and may present with or without dacryocystitis. This higher prevalence of primary acquired nasolacrimal duct obstruction in women may be secondary to their narrower nasolacrimal ducts, and, or the possible hormonal effects on its mucosa leading to obstruction. There is an increased incidence of dacryocystitis in females (71.3%).[1]

Cicatricial nasolacrimal duct drainage obstruction has been reported to result from various medical therapies, both topical and systemic medications, radiation, systemic chemotherapy, and bone marrow transplantation.

Patients with Down's syndrome have been noted to develop a dacryostenosis, more frequently caused by anatomic abnormalities, canalicular stenosis, and atresia. Punctal atresia and canalicular obstruction are also more common in patients with midface abnormalities.

Bartley modified the Linberg and McCormick etiologic classification system for "primary acquired nasolacrimal duct obstruction" (PANDO), and published an expanded classification for "secondary acquired lacrimal drainage obstruction" (SALDO). The etiologies causes of SALDO were divided into five categories: infectious, inflammatory, neoplastic, traumatic, and mechanical[2] (Table 5.1).

Location of Stenosis or Occlusion

Punctum and/or Vertical Canaliculi

Acquired stenosis or occlusion of the punctum and canaliculi may be caused by a variety of conditions, including inflammatory conditions, infections, trachoma, cicatrizing diseases of the conjunctiva, that are secondary to the toxic effect of topical or systemic medications, especially systemic chemotherapeutic medications, masses in the area of the punctum, surgery, burns, trauma, long-standing ectropion or lid malposition, aging changes, blepharitis, trauma, tumors, or iatrogenic response.

Punctal stenosis is more common in postmenopausal women, probably secondary to hormonal changes. Chronic blepharitis causes inflammatory and cicatricial changes resulting in inflammatory membrane formation, conjunctival epithelial overgrowth, and keratinization of the walls of the punctum. Membranous stenosis at the internal punctum is the most common location for canalicular stenosis. Involutional changes of these tissues, atrophy, and dense fibrous stricture of the punctum cause it to be less resilient and the orbicularis muscle fibers to become atonic and stenotic.

Conjunctivochalasis, excess conjunctiva that occludes the inferior punctum, is often overlooked. In mild cases, it may cause tearing because of tear film instability; in moderate cases, it may cause

TABLE 5.1. Causes of secondary acquired nasolacrimal duct obstruction.

Neoplastic
  Primary
  Secondary
  Metastatic
  1. **Primary neoplasms**
      a. Adenocarcinoma
      b. Adenoid cystic carcinoma
      c. Angiofibroma
      d. Angiosarcoma
      e. Cavernous hemangioma
      f. Cyst
      g. Dermoid cyst
      h. Fibroma
      i. Fibrous histiocytoma
      j. Glomus tumor
      k. Granular cell tumors
      l. Hemangioendothelioma
      m. Hemangiopericytoma
      n. Leukemia
      o. Lymphoma
      p. Lymphoplasmacytic infiltrate
      q. Melanoma
      r. Mucoepidermoid carcinoma
      s. Neurilemoma
      t. Neurofibroma
      u. Oncocytic adenocarcinoma
      v. Oncocytic adenoma
      w. Oncocytoma
      x. Papilloma and inverted papillomas
      y. Plasmacytoma
      z. Pleomorphic adenoma
      aa. Pyogenic granuloma
      bb. Squamous cell carcinoma
      cc. Transitional cell carcinoma
  2. **Secondary involvement by neoplasm**
      a. Adenoid cystic carcinoma
      b. Amyloid
      c. Basal cell carcinoma
      d. Capillary hemangioma
      e. Esthesioneuroblastoma
      f. Fibrosarcoma
      g. Fibrous dysplasia
      h. Intraosseous cavernous hemangioma
      i. Leukemia
      j. Lymphoma
      k. Maxillary and ethmoid sinus tumors
      l. Midline granuloma
      m. Mucoepidermoid carcinoma
      n. Mycosis fungoides
      o. Neurofibroma
      p. Osteoma
      q. Papilloma
          i. Conjunctival
          ii. Inverted (schneiderian)
      r. Rhabdomyosarcoma
      s. Sebaceous gland carcinoma
      t. Squamous cell carcinoma
  3. **Metastatic**
      a. Breast carcinoma
      b. Melanoma
      c. Prostate carcinoma

TABLE 5.1. *Continued*

Inflammations
1. **Endogenous**
    a.   **Wegener's granulomatosis and other forms of vasculitis**
    b.   **Sarcoidosis and sarcoid granuloma**
    c.   **Cicatricial pemphigoid**
    d.   **Stevens-Johnson syndrome (erythema multiforme)**
    e.   **Sinus histiocytosis**
    f.   **Orbital inflammatory syndrome (pseudotumor)**
    g.   **Kawasaki's disease (mucocutaneous lymph node syndrome)**
    h.   **Porphyria cutanea tarda**
    i.   **Epidermodysplasia verruciformis, ichthyosis, scleroderma**
    j.   **Idiopathic punctal stenosis**
    k.   **Benign squamous metaplasia**
    l.   **Sjögren's syndrome**
    m.   **Lichen planus**
2. **Exogenous**
    a.   **Eyedrops**
        i.   **Antiviral agents**
            1. **Idoxuridine**
            2. **Vidarabine**
            3. **Trifluridine**
            4. **Acyclovir**

        ii.   **Antiglaucoma medications**
            1. **Demecarium**
            2. **Echothiophate**
            3. **Isoflurophate**
            4. **Furmethide**
            5. **Neostigmine**
            6. **Physostigmine**
            7. **Epinephrine**
        iii.   **Silver nitrate, silver protein, colloidal silver**
        iv.   **Thiotepa**
    b.   **Radiation therapy**
    c.   **Fluorouracil (systemic)**
    d.   **Graft-versus-host disease**
    e.   **Pyogenic granuloma**
    f.   **Foreign body granuloma**
    g.   **Allergy**
        i.   **Ocular**
        ii.   **Nasal**
    h.   **Burns**
        i.   **Thermal**
        ii.   **Chemical**
    i.   **Chronic sinus disease**

Infections
1. **Bacterial**
    a.   *Actinomyces* **sp.**
        (1)   *A. israelii*
        (2)   *A. meyeri*
    b.   *Propionibacterium propionicum* (*Arachnia propionica*)
    c.   *Fusobacterium* **sp.**
    d.   *Bacteroides* **sp.**
    e.   *Mycobacterium* **sp.**
        (1)   *M. fortuitum*
        (2)   *M. leprae*
        (3)   *M. tuberculosis*
    f.   *Chlamydia trachomatis*
    g.   *Nocardia asteroides*
    h.   *Enterobacter cloacae*
    i.   *Aeromonas hydrophila*
    j.   *Treponema pallidum*

TABLE 5.1. *Continued*

    k. *Staphylococcus aureus*
    l. *Staphylococcus epidermidis*
    m. *Pseudomonas aeruginosa*
    n. *Proteus mirabilis*
    o. *Haemophilus influenzae*
    p. *Peptostreptococcus*
    q. *Streptococcus viridans*
    r. Gamma streptococcus
    s. Diphtheroids
    t. *Klebsiella*
    u. *Moraxella*
    v. Mononucleosis
    w. *S. pneumoniae*
    x. *Escherichia coli*
    y. *N. gonorrhea*
    z. *N. catarrhalis*
    aa. Trachoma
    bb. Leprosy
    cc. Tuberculosis
 2. Viral
    a. Herpes simplex virus
    b. Herpes zoster virus
       i. Varicella
    c. Smallpox
    d. Adenovirus
    e. Vaccinia virus
    f. Epstein-Barr virus
    g. Human papillomavirus
 3. Fungal
    a. *Aspergillus* sp.
       i. *A. fumigatus*
       ii. *A. niger*
    b. *Candida* sp.
       i. *C. albicans*
       ii. *C. parapsilosis*
    c. *Pityrosporum* sp.
       a. *P. orbiculare*
       b. *P. pachydermatis*

    d. *Rhinosporidium seeberi*
    e. *Sporothrix schenckii*
    f. *Streptomyces somaliensis*
    g. *Trichophyton rubrum*
    h. Cephalosporiosis
    i. Blastomycosis
    j. Cryptococcosis
 4. Parasitic
    a. *Ascaris lumbricoides*
    b. *Distoma felineum*
    c. Myiasis

Traumatic
 1. Iatrogenic
    a. Punctal occlusion for dry eyes
    b. After nasolacrimal duct probing with or without silicone
       intubation
    c. After canalicular repair with pigtail probe
    d. After dacryocystorhinostomy
    e. After conjunctivodacryocystorhinostomy
    f. After transantral orbital decompression
    g. After sinus surgery (conventional or endoscopic)
    h. After rhinoplasty, rhinotomy, or other nasal surgery
    i. After craniofacial surgery

TABLE 5.1. *Continued*

  2. **Noniatrogenic**
    a. **Laceration of canaliculus**
    b. **Laceration of lacrimal sac**
    c. **Fractures involving nasolacrimal duct nasoethmoid fractures, midfacial trauma**

Mechanical
  1. **Internal**
    a. **Dacryolith**
      i. **Idiopathic**
      ii. **Eyelash nidus**
      iii. **Epinephrine cast**
      iv. **Quinacrine deposits**
    b. **Migrated or retained medical device**
      1. **Punctal plug**
      2. **Veirs rod**
      3. **Fragment of nasolacrimal probe**
      4. **Modified myringotomy tube**
      5. **Remnants of silicone tubing**
    c. **Pellet (BB)**
    d. **Canalicular cysts**
    e. **Blood**
  2. **External**
    a. **Kissing puncta**
    b. **Conjunctivochalasis; enlargement of the plica, semilunaris, and/or caruncle**
    c. **Mucocele**
    d. **Migrated or malpositioned orbital floor or medial wall implants after repair of orbital floor or medial wall fractures**
    e. **Paget's disease**
    f. **Osteopetrosis**
    g. **Rhinolith or other nasal foreign bodies**
    h. **Suture stent after esophagocolostomy**
    i. **Exudative rhinitis**
    j. **Acute intranasal inflammation**
    k. **Nasal mucosal edema**
    l. **Lymphoid hyperplasia of the nasal cavity**
    m. **Nasal malformations**
    n. **Nasal polyps or polyposis**
    o. **Systemic syndromes or dysmorphism that involve abnormalities of facial development (clefting or malposition of the orbits or midface)**
    p. **Intranasal tumors**
    q. **Impacted turbinate**
    r. **Intranasal tumors**

Source: Modified from Linberg JV, McCormick SA. Primary acquired nasolacrimal duct obstruction: a clinicopathologic report and biopsy technique. Ophthalmology 1986; 93:1055–1062; and Bartley.[2,9]

obstruction of the puncta, and in severe cases, it may cause foreign body sensation and irritation that result from ocular surface exposure.

    Obstruction may occur within either the upper or lower canaliculus or in the common canaliculus. Causes of acquired canalicular obstruction include trauma and toxicity from medications (5-fluorouracil, idoxuridine, phospholine iodide, eserine, etc.).

Canalicular obstructions may be caused by chlamydial infections (trachoma), viruses (herpes zoster, herpes simplex, chickenpox, and smallpox), bacteria, or cicatrizing diseases (Stevens-Johnson syndrome or pemphigoid).

Canalicular cyst presents as a bluish lump or a cyst-like swelling. These cysts may arise after an episode of canaliculitis with an ecstatic canalicular diverticulum, an encysted abscess, or chronic canaliculitis.

Lacrimal Pump

The lacrimal pump is the mechanism that assists the tears in their travels from the tear pool through the nasolacrimal duct system into the interior meatus of the nose. The action of the pretarsal and pre-septal orbicularis oculi produces the forces that drive the lacrimal pump.

Patients with tearing whose nasolacrimal duct systems are patent to syringing may have an incomplete anatomic obstruction or nonfunctional segments of the lacrimal passage from prior episodes of dacryocystitis, or an anatomically normal nasolacrimal duct system, but a physiologic dysfunction of the eyelids, punctum, lacrimal pump, or a lacrimal sac that drains poorly.

Lacrimal Sac and Duct

The mucosal lining of the nasolacrimal sac and duct excretes a range of mucin materials, which may aid in the flow of tears and provide a defense against microbes. Researchers have identified mRNA for a variety of mucins in human lacrimal sacs and ducts.[3]

Inflammation, trauma, or congenital defect in the drainage system may cause epiphora, dacryostenosis, and dacryocystitis. Inflammation originating at the eye, conjunctival sac, diverticula of the lacrimal system, or from the nose, infections or diseases of the nasal mucous membrane or sinuses can induce swelling of the lacrimal system's mucous membranes, resulting in narrowing or occlusion of the nasolacrimal system from the epithelial changes and fibrosis of the lamina propria.[4] The various mechanisms that cause inflammation result in a secondary fibrosis that causes a narrowing of the nasolacrimal duct system, and eventually, occlusion by scar tissue. The lacrimal sac and duct undergo similar changes, as the pseudostratified, ciliated, columnar epithelium undergoes squamous metaplasia and hyperplasia with loss of goblet cells, and ulceration. The underlying mucosa develops a secondary fibrosis. Basement membrane thickening may develop in the nasal mucosa but not in the lacrimal sac. The inflammation may cause a fibrosis of the lacrimal sac and the internal common punctum, which may result in obstruction and, in postoperative cases, to failure of dacryocystorhinostomies.[5]

Several valves are present in the nasolacrimal duct system to prevent the retrograde flow of tears. The most important valve clinically is the valve of Hasner, located at the entrance of the nasolacrimal duct into the inferior meatus, and frequently responsible for congenital nasolacrimal duct obstruction. The valve of Rosenmüller is found at the junction of the common canaliculus into the lacrimal sac. This valve prevents retrograde flow of fluid from the sac into the canaliculi and fornix. In episodes of dacryocystitis, this valve may swell closed even more tightly. Tears and the infection cannot drain out of the sac into the nose, or to the fornix. The valve of Rosenmüller is not a true valve, but an angulated entrance of the common canaliculus into the sac, functioning as a valve.

Descending inflammation from the eye or ascending inflammation from the nasal cavity may initiate swelling of the mucous membranes of the nasolacrimal duct system, remodeling of the helical arrangement of connective tissue fibers, malfunctions in the subepithelial cavernous body with reactive hyperemia, and temporary occlusion of the nasolacrimal duct system. The submucosa is very vascular, cavernous in structure, and rich in lymphatics, so that a slight infection, once established, will settle. The constriction of the tissue within the bony canal makes it obligatory that any swelling will lead to blockage. The submucosa of the nasolacrimal duct system surrounded by bone contains arterioles with sphincters and cavernous vessel complexes, which can cause swelling and approximation of the lumen according to the blood flow. Repeated episodes of dacryocystitis will result in permanent changes of the epithelial and subepithelial tissues; loss of goblet and epithelial cells, which are important in the tear outflow mechanism; fibrosis of the helical system of connective tissue fibers; and reduction and destruction of the vascular plexus, leading to a malfunction of the tear flow mechanism – all of which result in a vicious circle.[6] These structural epithelial and subepithelial changes may lead either to a total fibrous closure of the lumen of the nasolacrimal duct system or to a nonfunctional segment that may cause chronic epiphora and discharge, but be patent to irrigation.

Dacryocystitis has various causes, but the common end result is complete obstruction of the nasolacrimal duct, resulting in stasis of tear flow, leading to secondary infections, which may progress to mucocele, pyocele-mucocele, chronic conjunctivitis, preseptal and orbital cellulitis, and abscess formation if left untreated, or if inadequately treated. Gram-positive bacteria are the most common cause, but gram-negative organisms should be suspected in patients with diabetes or who are immunocompromised.

The lacrimal sac can be involved by inflammation, the most common being nongranulomatous inflammation, granulomatous inflammation, granulation tissue, lymphocytic infiltrate, inflammation and ulcerations, and sarcoidosis. The epithelial lesions that involve the lacrimal sac are inverted papilloma, papilloma, transitional cell carcinoma, oncocytoma, granular cell tumor, carcinoma, and adenocarcinoma. The nonepithelial lesions are lymphoma, lymphoplasmacytic infiltrate,

plasmacytoma, and chronic lymphocytic leukemic. Infections that involve the lacrimal sac can be secondary to fungus, *Actinomyces*, and bacteria. The lacrimal sac can also be affected by dacryoliths, scarring, foreign bodies, pyogenic granulomas, amyloid, orbital and midfacial fractures, blood, trauma, and papillary hyperplasia.

Lacrimal diverticula, outpouchings of the canaliculi or the lacrimal sac, are rare but may cause intermittent or permanent swelling near the lacrimal sac. Most arise from the lateral sac wall, because this area is only covered by the periorbita, offering little resistance to distention of the sac. They may be congenital, inflammatory, result from prior dacryocystitis, or be traumatic in origin. This communication may be open or act as a one-way valve, becoming symptomatic, and may cause epiphora, swelling, and/or dacryocystitis-like symptoms. Dacryoliths may form inside the diverticulum.

Obstruction of the intraosseous segment of the nasolacrimal duct may be secondary to trauma, chronic sinus disease, granulomatous disease (Wegener's granulomatosis, sarcoidosis, and lethal midline granuloma), dacryocystitis, or involutional stenosis. Involutional stenosis is probably the most common cause, seen more frequently in older women.

Obstruction of the Nasal Portion of the Nasolacrimal Duct

Mechanical obstruction is frequently found with enlargement or flattening of the inferior turbinate, which may almost obliterate the anterior part of the meatus and may cause a local rhinitis. A deviated septum may compress the inferior turbinate against the lateral nasal wall.

Inflammatory conditions, chronic nasal catarrh, acute and suppurative infections, may spread into the inferior portion of the nasolacrimal duct, resulting in obstruction. Atrophic and destructive conditions of the nasal mucosa may create a patulous ostium permitting extension of the disease process upward and allowing the direct entrance of infective secretion into the duct on blowing the nose.

Congestive and hypertrophic conditions of the mucosa, vasomotor or inflammatory, may cause obstruction at or in the inferior portion of the nasolacrimal duct, as well as a nasal polyp or neoplasm. Dacryocystitis has also been reported after packing of the nose.

Intranasal pathology may affect the nasolacrimal duct. Intranasal scarring with inferior turbinate adhesions that occur from trauma, radiation therapy, surgical procedures, or nasal mucosal hypertrophy from allergic rhinitis may cause obstruction of the duct.

Etiologic Causes

Infectious

The infectious causes of PANDO may be secondary to bacteria, viruses, fungi, and parasites. Generalized infections are occasionally responsible for the onset of dacryocystitis, as seen with the occurrence of

inflammation during the course of influenza, scarlet fever, diphtheria, chickenpox, smallpox, and tuberculosis.

The occurrence of acute dacryocystitis is dependent on the entry of a virulent strain of an organism into the stagnant contents of a lacrimal sac where the nasolacrimal duct is obstructed. Chronic dacryocystitis may be primary or secondary to an anatomic abnormality that has led to tear flow stasis. Obstructed lacrimal duct systems are colonized by increased numbers of pathogenic microorganisms. Some cases of PANDO may be secondary to unrecognized low-grade dacryocystitis. The organisms in the lacrimal sac may contribute to inflammation and scarring and therefore to the obstruction and then dacryocystitis. The microbiology of acute dacryocystitis has been reported to be frequently secondary to species of staphylococcus, streptococcus, pneumococcus, and *Staphylococcus pyogenes*, with mixed infections being common. The most frequently cultured organisms were *S. epidermidis* and *S. aureus*. The common gram-negative rods include *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Enterobacter cloacae*, and *Haemophilus influenzae*. Frequently, in these studies, cultures were interpreted from the cul-de-sac or from cases of chronic dacryocystitis and therefore may not have accurately identified the causative organism. Studies have shown that there is not a significant correlation between organisms cultured from the lacrimal sac to those obtained from the conjunctiva and/or nose; therefore, the preoperative conjunctival and/or nose cultures do not accurately predict the causative organism of the dacryocystitis.[7]

The viruses of primary herpes simplex, herpes zoster, chickenpox, smallpox, vaccinia, epidemic keratoconjunctivitis, and Epstein-Barr viruses may cause inflammatory and cicatricial changes of the canaliculi, resulting in varying degrees of obstruction or occlusion. These infections can extend beyond the stratified squamous epithelium to involve the elastic tissue of the substantia propria rather than the canalicular epithelium alone, or because of the adherence of the raw surfaces caused by inflammation of the mucous membranes, resulting in stenosis. Bacterial infections do not frequently affect the elastic layer. During the first few weeks of these viral infections, the mucosal epithelium is edematous, causing a stenosis that will still be able to be probed. The cicatrization that occurs over the next several weeks to months generally causes an obstruction that involves the mid-zone or distal portions of the superior and inferior canaliculi, but occasionally may cause punctal occlusion. Early recognition, probing, and intubation when indicated can prevent permanent canalicular obstruction and the need for a conjunctivodacryocystorhinostomy.

Infectious mononucleosis, mumps, Nicolas-Favre lymphogranulomatosis, trachoma, Stevens-Johnson syndrome, and pemphigus may cause dacryostenosis.

Dacryocystitis has been reported to result from infections with several species of mycobacteria: *Mycobacterium fortuitum*, *M. leprae*, and *M. tuberculosis*.

Chlamydia trachomatis has been reported to cause punctal occlusion, canalicular scarring, and nasolacrimal duct obstruction.

Other bacteria associated with lacrimal drainage obstruction include *Nocardia asteroides*, *E. cloacae*, *Aeromonas hydrophila*, *Treponema pallidum*, and *S. aureus*.

Fungi generally occlude the lacrimal drainage system by the formation of stone or cast. *Aspergillus fumigatus*, *A. niger*, *Candida albicans*, *C. parapsilosis*, *Pityrosporum orbiculare*, *P. pachydermatis*, *S. somaliensis*, *Actinomyces*, and *Trichophyton rubrum* may cause lacrimal stones or casts.

Parasitic obstruction is unusual, but has been reported with the nematode *Ascaris lumbricoides*. The worm gains entrance to the nasolacrimal system through the valve of Hasner and then emerges from the punctum.

Verruca vulgaris and viruses may cause a bloody epiphora when they involve the punctum or canaliculus.

Nocardia, sporotrichosis, rhinosporidiosis, cephalosporiosis, *Pseudomonas*, *Candida*, *Aspergillus*, which is commonly associated with other bacteria, *H. influenzae*, *Treponema vincentii*, *Rhinosporidium seeberi*, *Sporothrix* fungus, as well as *Treponema*, and tuberculosis, have been reported to cause dacryocystitis.

Actinomyces, previously named *Streptothrix israelii*, an obligate parasite whose only host is humans, causes a canalicular obstruction and inflammation. *Actinomyces israelii* is a gram-positive aerotolerant rod with true branching, which causes inflammation rather than a blockage of the lacrimal duct. Most cases of canaliculitis are unilateral. *Actinomyces* organisms are sensitive to penicillin, but topical antibiotic therapy is usually ineffective without mechanical expression or surgical removal of the canalicular stones.

Dacryoliths are typically yellow or white, "sulfur granules" and are frequently secondary to *Actinomyces* organisms, but may occasionally be seen in infections secondary to *Nocardia*, *Streptomyces*, and *Staphylococcus*. Shed epithelial cells, amorphous debris, and lipids with or without calcium can form casts within the lacrimal sac, which can lead to obstruction. In addition to the above, casts have been reported to form from the oxidation products of long-term topical epinephrine use.

Canaliculitis

Canaliculitis may be caused by a variety of bacterial, viral, chlamydial, or mycotic organisms. *A. israelii* is a filamentous gram-positive rod that is reported as one of the most common causes. *Propionibacterium propionicum* – formerly *Arachnia propionica* – is gram-positive and has a branching, rod-shaped morphology. It is facultatively anaerobic; carbon dioxide is not necessary for growth, unlike with *Actinomyces*. *Fusobacterium*, *A. israelii*, and *Bacteroides* have also been cultured from cases of canaliculitis.

A. Meyeri is principally found in the periodontal sulcus, is an uncommon pathogen, is nonfilamentous, branching, may be difficult to demonstrate, and can cause canaliculitis.

Fungi generally occlude the lacrimal drainage system by the formation of stone or cast, which can be seen with *A. fumigatus*, *A. niger*,

C. albicans, C. parapsilosis, P. orbiculare, P. pachydermatis, S. somaliensis, Actinomyces, and *T. rubrum*.

Inflammatory

Inflammation caused by numerous diseases may cause narrowing or obstruction of the nasolacrimal system.

Endogenous Origin

Granulomatous diseases can occasionally produce a mass within the lacrimal sac, as seen with extraorbital manifestations of idiopathic orbital inflammatory syndrome (idiopathic inflammatory pseudotumor) and sarcoidosis. In patients with sarcoidosis, and the other inflammatory diseases, initially successful dacryocystorhinostomy has an increased incidence of late failure caused by the progression of the inflammation in the nasal and lacrimal sac mucosa.

Wegener's granulomatosis, a vasculitis that classically involves the triad of the upper respiratory tract, the lungs, and the kidneys, may cause obstruction of the nasolacrimal system. Nasolacrimal obstruction is typically associated with advanced nasal disease, late in the disease process. This obstruction is frequently secondary to contiguous nasal disease, but may also be secondary to a vasculitis of the lacrimal sac mucosa. Treatment of the nasolacrimal obstruction should be deferred until the inflammation is quiescent, if possible. Other forms of vasculitis may cause similar obstructions of the nasolacrimal duct system.

Cicatricial pemphigoid and Stevens-Johnson syndrome may cause nasolacrimal obstruction with advanced disease.

Sinus histiocytosis, a benign disease of unknown etiology, which may be related to an allergy or an immunologic abnormality of histiocytes, Kawasaki's disease (mucocutaneous lymph node syndrome), thyroid disease, and Sjögren's syndrome may cause nasolacrimal obstruction.

Punctal stenosis may occasionally occur spontaneously. The punctum may become stenotic with cicatricial diseases affecting the eyelid margin. Chronic punctal eversion may also result in stenosis of the puncta. Obstruction of the proximal sac or common canaliculus has been reported with epidermodysplasia verruciformis, ichthyosis, scleroderma, and the sclerodermoid variant of porphyria cutanea tarda. Lower lid ectropion, which often has an inflammatory or cicatricial component, and may be associated systemic diseases, has been reported occasionally to be associated with dacryostenosis.[8]

Lichen planus, an immune-mediated skin and mucosal disease similar to pemphigoid, may cause lacrimal stenosis and obstruction. There is a cell-mediated reaction at the level of the epithelial basement membrane. This may also cause a cicatrizing conjunctivitis with shortening of the fornices, symblepharon formation, and a keratitis.

Exogenous Factors

It is important to remove all remnants of silicone tubing from the lacrimal system to prevent secondary obstruction caused by inflamma-

tory masses, because the mucosal surfaces are prone to the development of granulation tissue, pyogenic granuloma and true granulomas, and nongranulomatous reactions to the silicone tube may occasionally occur.

Ocular and periocular disorders, such as atopic disease, sinus and nasal inflammations, exudative rhinitis, and allergies, may develop into nasolacrimal stenosis and obstruction.

Allergic conjunctivitis in patients who chronically rub their eyes can cause an intermittent allergic obstruction at the level of the puncta, canaliculus or lacrimal sac, which may progress to a permanent occlusion.

Tumors (Neoplastic)

The insidious nature of lacrimal sac tumors may present as dacryostenosis or dacryocystitis. The mass is usually above the medial canthal tendon. The position of the medial canthal tendon does not frequently allow distention of the sac by fluid, or distention from dacryocystitis superior to the tendon. A tumor within the sac can create a mass effect above the tendon. Therefore, any distention of the lacrimal sac superior to the medial canthal tendon should be considered to be a tumor until proven otherwise. The dacryocystitis symptoms produced may differ from other causes of dacryocystitis, in that the irrigation fluid may pass into the nose or blood may reflux from the punctum, other factors may be telangiectasia and regional lymphadenopathy. Intermittent epiphora, sanguineous discharge, or an irreducible mass should always lead one to suspect a lacrimal sac tumor.

Approximately 45% of lacrimal sac tumors are benign and 55% are malignant. There have been cases reported in which the initial symptoms of epiphora, or dacryocystitis were found at surgery to be secondary to tumors. Squamous cell papillomas and carcinomas are the most common. Many papillomas initially grow in an inverted pattern into the lacrimal sac wall and therefore are often incompletely excised. Recurrence and malignant degeneration can occur.

Primary tumors of the nasolacrimal duct system are uncommon, but can arise from within the puncta, canaliculi, lacrimal sac, nasolacrimal duct, or about its entrance into the nasal cavity, at the valve of Hasner. The epithelial tumors account for 75% of the lacrimal sac tumors, and the nonepithelial tumors for 25%, which include mesenchymal tumors, melanoma, malignant lymphomas, and leukemia, particularly in older patients with chronic lymphocytic leukemia. Secondary tumors and metastatic lesions can infiltrate or compress the nasolacrimal system, resulting in symptoms of dacryostenosis and dacryocystitis that are much more common than primary tumors. The secondary tumors include adenoid cystic carcinoma, basal cell carcinoma, capillary hemangioma, esthesioneuroblastoma, fibrous dysplasia, fibrosarcoma, intraosseous cavernous hemangioma, leukemia, lymphoma, lymphomatous diseases, mucoepidermoid carcinoma, osteomas, conjunctival papillomas, inverted papillomas, sebaceous gland carcinoma, squamous cell carcinoma, and rhabdomyosarcoma.

The most common primary tumors of the nasolacrimal system of epithelial origin are papillomas and squamous cell carcinomas. Less frequent ones are adenoid cystic carcinoma, angiofibroma, angiosarcoma, cavernous hemangioma, dermoid cyst, fibroma, fibrous histiocytoma, hemangioendothelioma, hemangiopericytoma, lacrimal sac cyst, lymphoma, melanoma, mucoepidermoid carcinoma, neurofibroma, neurilemoma, oncocytic adenoma, oncocytic adenocarcinoma, pleomorphic adenoma, dermatofibrosarcoma protuberans, neurilemoma, adenocanthoma, and more often involve the lacrimal sac. Schwannoma, fibrous histiocytoma, leukemia, and granulocytic sarcoma may infiltrate the lacrimal sac.

The most common neoplasms of the lacrimal sac are epithelial tumors. The most common benign epithelial tumor is a papilloma. Papillomas exhibit epithelial papillomatosis and acanthosis, and an inflammatory papilloma exhibits granulomatous tissue. Inverted papillomas can arise *de novo* in the lacrimal sac or more frequently from an extension of the lateral aspect of the nasal cavity or maxillary sinus. The lesion is not malignant but has a high recurrence rate. Metaplastic transformation to squamous cell carcinoma occurs in 10%–15% of cases, and therefore should be treated as a malignant lesion. The other forms of lacrimal sac epithelial carcinomas are less common. These include adenocarcinoma and epidermoid carcinoma. Mucoepidermoid carcinoma is a very aggressive cancer but is also rare.

The surrounding vascular plexus, which is in a system of collagen bundles, elastic, and reticular fibers arranged in a helical pattern, and the mucosa of the nasolacrimal duct system may be an area where leukemic or lymphomatous tumors may form primary or metastatically from hematologic spread because of their mucosal-associated lymphoid tissue; and frequently occur the tumors more in the middle-aged or elderly. Epiphora will often be the first complaint, before a mass develops or dacryocystitis occurs, and the system may remain patent to probing and irrigation. These lesions usually respond to local irradiation, stenting of the nasolacrimal duct system, and/or chemotherapy.

Lymphoproliferative diseases may involve the nasolacrimal system leading to epiphora, acute or chronic dacryocystitis. They are the second most common type of tumor causing nasolacrimal obstruction. Lymphomas are more frequent than benign lymphoproliferative lesions. Lymphosarcomas, reticulum cell carcinomas, and Hodgkin's disease have been reported to occur in the lacrimal sac.

The most frequent secondary tumors are eyelid lesions, particularly basal cell carcinoma, then squamous cell carcinoma, and less frequently, sebaceous cell carcinoma, which can involve the medial canthal region and the nasolacrimal duct system or can cause pressure and compression and the resultant dacryostenosis and dacryocystitis. The most frequent maxillary sinus lesion is squamous cell carcinoma. The most common lesions arising from the nasopharynx are lymphomatous and squamous cell carcinomas. Metastatic disease as a cause of dacryostenosis and/or dacryocystitis is very rare; lymphoma is the most common, but cases secondary to prostate carcinoma, breast carcinoma, and malignant melanoma have been reported.[9]

Both benign and malignant tumors of mesenchymal elements, capillary and cavernous hemangiomas, and hemangiopericytomas have been reported to involve the lacrimal sac. Melanomas, neurilemoma, plexiform neuroma, and osteoma can involve the lacrimal sac both intrinsically and extrinsically. Fibromas, Kaposi's sarcoma, and other sarcomas can rarely involve the lacrimal sac.

Sinus tumors invade the orbit and nasolacrimal duct system and can be benign or malignant. The benign lesions include inverted papillomas, osteomas, juvenile angiofibromas, and neuroectodermal tumors. Inverted papilloma is the second most common lesion that invades the orbit after squamous cell carcinoma. Inverted papillomas can arise from the lateral nasal wall or the mucosa of the ethmoidal sinus. Mucoceles of the paranasal sinuses can invade the orbit and cause nasolacrimal obstruction. Squamous cell carcinoma, adenocarcinoma, adenoid cystic carcinoma, esthesioneuroblastoma, lymphoma, and melanoma can occur in the paranasal sinus and rare tumors of the odontogenic tumors, which include ameloblastoma and ameloblastic fibrosarcoma, as well as fibrosarcoma, chondrosarcoma, sinus glioblastomas multiforme, and mucoepidermoid carcinoma and may cause dacryostenosis. The most frequent sinus tumor is squamous cell carcinoma of the maxillary sinus, then lymphomas, adenocarcinoma, adenoid cystic carcinoma, transitional cell carcinoma, olfactory neuroblastoma, osteoblastoma, and malignant histiocytosis.

When neoplasms are excised in the medial canthal area, complete resection must be performed and histopathologically controlled (frozen borders or Mohs technique). This includes any portion of the nasolacrimal system involved. The canaliculi may be marsupialized, but dacryocystorhinostomy or canaliculodacryocystorhinostomy should be delayed for 5 or more years to ensure that there are no recurrences and to decrease the morbidity and mortality.

Traumatic

Thermal or chemical burns may cause inflammation, dacryostenosis, and obstruction. Blunt trauma or lacerations usually damage the canaliculus, the lacrimal sac, or the nasolacrimal duct. The dense fibrous tissue of the tarsus is much stronger than the medial canalicular portion of the eyelid; therefore, any tractional force along the eyelid margin can result in avulsion of the medial eyelid with canalicular involvement. All canalicular lacerations should be repaired within 1 day of the injury, to prevent scarring and epithelialization of the wound.

Midfacial trauma and the resultant facial fractures frequently involve the bone about the lacrimal sac fossa, and/or nasolacrimal ducts, leading to obstruction of the nasolacrimal system. Fractures involving the distal portions of the nasolacrimal duct include the midface fractures of naso-orbital, LeFort II, and LeFort III fractures. It is always important to consider and evaluate the patient for involvement of the nasolacrimal duct with these types of fractures rather than waiting for the patient to present with epiphora and/or dacryocystitis. Even if lac-

rimal irrigation is easy and disappearance of fluorescein dye normal, only lacrimal duct probing can identify and define the extent of injury in these cases, because the fluid may pass into the nose through bony and membranous defects. Direct repair of these injuries is not possible, but stent placement will help to promote patency. Prophylactic intubation with silicone tubing should be considered to prevent this occlusion when indicated. Bony fractures may also initiate an inflammatory and cicatrizing reaction that may result in nasolacrimal duct obstructions shortly after or years after the injury.

Iatrogenic Obstruction

Dacryostenosis and obstruction may result from many procedures, such as repeated and traumatic probing of the canalicular system. Poor technique in the probing of the nasolacrimal ducts may cause the creation of a false passage and subsequent scarring of the lacrimal drainage system.

The pigtail probe has frequently been reported to cause iatrogenic damage to the nasolacrimal duct system, and many consider it to be a potentially harmful device. There have been reported cases of treatment of a single canalicular laceration, or congenital agenesis of only one punctum/canaliculus with the pigtail probe that resulted in obstruction of both canaliculi, which will then commit the patient to a conjunctivodacryocystorhinostomy.

Cheese wiring of silicone intubation tubes through the puncta, as well as nasal migration with complete healing of the eroded puncta and canaliculus, can occur. The erosion of the punctocanaliculi may also be the result of chronic irritation by the tubes, or tubes that were placed under tension. The tubes may be colonized with bacteria, including atypical *Mycobacterium*.

Punctal occlusion, which is frequently performed for the treatment of dry eye syndrome, keratoconjunctivitis sicca, may subsequently cause epiphora in a few patients, and may less frequently cause dacryocystitis. Partial or complete dacryostenosis, pyogenic granulomas, intracanalicular migration, and canaliculitis have been reported after the placement of permanent punctal plugs.

Collared punctal plugs are designed to be removable, but there have been rare cases of these plugs fracturing during removal, with migration of the remainder of the plug into the lacrimal system. The intracanalicular plugs have been noted to cause pyogenic granulomas, indicating that they are associated with an inflammatory process that disrupts the normal cellular functions and can cause a fibrosis and reactive mass. They have also been hypothesized to facilitate the overgrowth of bacteria and a chronic canaliculitis that can result in canalicular obstruction which may erode through the canalicular mucosa, resulting in synechia, symptomatic lacrimal stenosis, or even the formation of fistula.[10]

Intracanalicular plugs used for the treatment of dry eye syndrome, which are implanted in the horizontal canaliculus, may be difficult to

remove and may be associated with significant lacrimal complications. It may be difficult to irrigate these intracanalicular plugs through the nasolacrimal system. Irrigation does not reliably flush these intracanalicular plugs from the nasolacrimal system. The collarless intracanalicular plugs theoretically can be flushed through the nasolacrimal system but are not recovered from the nose. Therefore, successful removal cannot be objectively documented. Their retention may act as a nidus for infection, inflammation, epiphora, canaliculitis, and eventually obstruction of the nasolacrimal duct system, with dacryocystitis. Distal migration of the plugs may require complicated canalicular surgery, dacryocystorhinostomy, or conjunctivodacryocystorhinostomy.

Herrick plugs may cause irreversible chronic adverse reactions with persistent inflammation and epiphora. They may cause destruction of the normal canalicular architecture, proliferative tissue reaction, pericanalicular fibrosis, granulomatous tissue, pyogenic granuloma, giant cells reaction, canaliculitis, dacryocystitis, and lymphocytic infiltration. This reaction will cause chronic epiphora and canaliculitis.

Dacryostenosis may occur after a dacryocystorhinostomy as a result of new or persistent stenosis at the common internal punctum or of an improperly fashioned osteotomy. Dacryocystorhinostomy failure may be the result of retained stenting material. Migrated medial or orbital floor implants, or poorly placed or secured medial or orbital floor implants, may cause an external compression or occlusion of the nasolacrimal sac and/or duct.

Transantral orbital decompression has been reported to cause obstruction of the nasolacrimal duct system, possible secondary to delayed scarring around the nasoantral window. Dacryostenosis and obstruction has been reported as a complication of nasal operations, paranasal sinus surgery, both endoscopic and conventional external procedures, and craniofacial procedures.

Nasoantral window procedures are generally placed at the most anterior–inferior portion of the maxillary sinus. If they are placed too high or too posterior, or if the nasolacrimal duct is in an anomalous position, damage to the duct may occur. The Ogura procedure of orbital decompression that removes the medial and floor of the orbital, through an antrostomy, may also cause damage to the lacrimal duct.

Mechanical

Mechanical compression or blockage of the nasolacrimal duct system can result from external compression or occlusion of the system from an intraluminal foreign body, hematoma, or stone. Direct occlusion or external compression may impede or block the canaliculi or nasolacrimal duct.

The most common cause of internal mechanical obstruction is dacryoliths. Some are secondary to fungal infections, but frequently the cause is indeterminate. There are cases reported in which an eyelash served as a nidus for formation of the dacryoliths. Others have postu-

lated that metabolic factors such as high calcium and phosphate levels within an obstructed lacrimal system may contribute to the formation of dacryoliths. Various medications, epinephrine, and quinacrine have been reported to contribute to the formation of casts of the nasolacrimal ducts.

The foreign bodies that may cause internal mechanical obstruction are generally migrated or retained medical devices, such as punctal plugs, or incompletely removed silicone tubing. Rarely, intranasal bleeding can cause a hematoma of the lacrimal sac and duct.

External factors may cause a mechanical obstruction of the lacrimal system. Opposing superior and inferior puncti may cause a proximal obstruction, as in ptosis. Redundancy of the bulbar conjunctiva, conjunctivochalasis, may cause a mechanical obstruction, epiphora, or foreign body sensation. Excision of an ellipse of the redundant conjunctiva is often curative.

Masses arising from the paranasal sinuses, nasal polyps, mucoceles, mucopyoceles, nasal mucosal edema, lymphoid hyperplasia of the nasal cavity, exudative rhinitis, or tumors may cause an external compress of the lacrimal sac or duct. Nasal mucosal edema and mucopurulent exudates may lead to obstruction of the nasolacrimal duct at the intranasal ostium, valve of Hasner. Allergic, viral, or bacterial pharyngitis and rhinitis can produce sufficient nasal mucosal edema, lymphoid hyperplasia, and exudates to result in obstruction of the nasolacrimal duct and progression to a dacryocystitis.

Lacrimal sac cysts, dacryops, are congenital or traumatic in origin. They grow slowly, and may present as a painless epiphora or dacryocystitis.

Maxillary sinus cysts, antral mucoceles, retention cysts, pseudocysts, dentigerous cysts and keratocysts, ameloblastoma, ossifying fibroma, giant cell granuloma, and cholesteatoma, may rarely lead to nasolacrimal obstruction.

Nasal malformations, systemic syndromes, or dysmorphisms that involve abnormalities of facial development, such as clefting or malposition of the orbits or midface, can be associated with maldevelopment of the nasolacrimal duct system. Patients with the centurion syndrome have an anterior displacement of the medial canthal tendon, a prominent nasal bridge, and displacement of the punctum away from the tear pool, resulting in epiphora.

Paget's disease and osteopetrosis have been reported as causes of acquired nasolacrimal obstruction.[11] Sarcoid granuloma, oncocytoma, rhinoliths, and nasal foreign bodies in the inferior meatus can cause a mechanical obstruction of the nasolacrimal duct system at the valve of Hasner.

A retrospective study of 377 dacryocystorhinostomy specimens demonstrated nongranulomatous inflammation (321, 85.1%), granulomatous inflammation consistent with sarcoidosis (8, 2.1%), lymphoma (7, 1.9%), papilloma (4, 1.11%), lymphoplasmacytic infiltrate (4, 1.1%), transitional cell carcinoma (2, 0.5%), and single cases of adenocarcinoma, undifferentiated carcinoma, granular cell tumor, plasmacytoma, and leukemic infiltrate. Neoplasms resulting in chronic nasolacrimal

duct obstruction occurred in 4.6% of cases and were unsuspected before surgery in 2.1% of patients.[12]

Punctal eversion, ectropion, or facial palsy may also impair the lacrimal pump action.

Medications

Acquired dacryostenosis may result from the use of antiviral, antiglaucoma, or systemic chemotherapeutic medications. The most common cause of iatrogenic punctal or canalicular stenosis and occlusion is ophthalmic medications. Idoxuridine, vidarabine, trifluridine, acyclovir, demecarium, echothiophate, isoflurophate, adenine arabinoside, furmethide, floxuridine, fluorouracil, neostigmine, physostigmine, epinephrine, pilocarpine, quinacrine, silver preparations, and thiotepa, have been most frequently associated with dacryostenosis and occlusion.

Idoxuridine, trifluridine, and adenine arabinoside generally cause occlusion of the punctum, rather than the mid-zone of the canaliculi as seen from viral infections. The punctal stenosis that occurs from antiviral toxicity will frequently reverse on discontinuation of the medication early on. The antiglaucoma medication may cause a cicatricial conjunctivitis that may be similar to, and indistinguishable from, cicatricial pemphigoid.

Chronic topical epinephrine may affect the vascular plexus of the nasolacrimal duct system. This specialized vascular system permits opening and closing of the lumen of the lacrimal passage, effected by the bulging and subsiding of the vascular system, which can regulate tear outflow.[13] Frequent topical cyclopentolate hydrochloride has been reported to cause dacryostenosis.

The systemic use of some antineoplastic agents, such as 5-fluorouracil and docetaxel has been reported to cause punctal and canalicular stenosis and occlusion with epiphora.[14]

Systemic 5-fluorouracil, a pyrimidine analog that blocks the enzyme thymidylate synthetase and docetaxel can cause obstruction of the nasolacrimal system, punctal and canalicular stenosis and obstruction. 5-fluorouracil may also cause lacrimation, conjunctivitis, blepharitis, keratitis, blurred vision, pain, ankyloblepharon, and cicatricial ectropion. It may cause an inflammatory response in mucosal membranes, as evident by conjunctivitis, as well as oral and gastrointestinal inflammation. The inflammation and fibrosis of the lacrimal drainage system causes extensive fibrous adhesions that obstruct the canaliculi and lacrimal sac.[15] These drugs and similar ones cause damage to the mucosal lining, which occasionally may cause permanent damage to the lacrimal system.

Docetaxel is an effective chemotherapeutic agent for advanced breast cancer and other common malignancies in the antineoplastic class of taxanes. Epiphora and permanent canalicular stenosis can occur in up to 50% of patients receiving weekly docetaxel and to a lower percentage in patients receiving docetaxel every 3 weeks. Chronic inflamma-

tion and extensive fibrotic changes have been demonstrated in the stroma of the lacrimal sac and the nasal mucosa. In advanced cases, this occlusion is not reversible. The mechanism of canalicular stenosis may be secondary to secretion of docetaxel in the tear film and fibrosis of the canaliculi from direct contact, or the mucous membrane lining of the puncta and canaliculi develop a fibrosis secondary to the systemic effects of the drug, similar to the widespread edema and fibrosis seen elsewhere in the body. Patients receiving docetaxel should be screened for epiphora and canalicular stenosis, and should receive treatment in the form of silicone intubation to prevent the need for a conjunctivodacryocystorhinostomy.[16] With the newer regimens that use lower doses of the drug for shorter periods than in the past, lacrimal stenosis and occlusion should be less frequent.

Radiation

External radiation in the treatment of neoplasia can cause inflammation of the lacrimal drainage system, stenosis, and occlusion. The reported dose in the literature has varied greatly, and it has been reported to occur in a case receiving as little as 1,800 rad (cGy). Other reports state that the lacrimal passages are relatively immune to radiation therapy until significantly higher doses are delivered. It has been hypothesized that the epiphora probably results from a combination of anatomic lacrimal obstruction, conjunctival epithelial alterations, damage to conjunctival epithelial cells, and damage to conjunctival goblet cells and glands. It is recommended that intubation be considered in patients undergoing radiation for medial canthal tumors. Topical corticosteroids may also be useful in preventing punctal stenosis.[17]

Cobalt and iridium brachytherapy have been reported to cause severe dermatitis and lacrimal drainage stenosis. Lovato et al.[17] reported a prospective study in which 11 of 12 patients that had prophylactic nasolacrimal intubation with silicone tubing maintained lacrimal duct patency, whereas 10 of 12 patients who did not receive prophylactic silicone intubation developed punctal occlusion after helium ion therapy for uveal melanoma.

Radioiodine ablation, I^{131} therapy for thyroid carcinoma at cumulative activities of 150 mCi of I^{131} or more, may produce clinically significant nasolacrimal drainage system obstructions in 4.6% of patients. The areas of obstruction involved the nasolacrimal duct, common canaliculus, and rarely, the superior and inferior canaliculi. The mechanism of the dacryostenosis may be a contribution of local toxicity from direct radiation injury from the passive flow of radioactive tears and/or active uptake and concentration of I^{131} in the nasolacrimal drainage tissues from the blood by the sodium/iodide symporter, the same iodine uptake mechanism used by the thyroid gland. This increased incidence of dacryostenosis and obstruction is likely to be dose-related. Symptomatic patients should receive early evaluation and treatment,

possibly with silicone tube placement, because once complete obstruction has developed, it has proven to be difficult to manage.[18]

It is hoped that these classification systems will be useful in the evaluation and treatment of nasolacrimal disorders. Determination of the location of the stenosis or occlusion, and the etiologic classification system presented above, provide a useful mechanism in the formulation of a differential diagnosis and help to develop the appropriate evaluation and treatment plan for each individual patient. These divisions may not be completely isolated; there will be cases that overlap; and there are some diseases and/or clinical situations that have not been included in this review.

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