the loss of WGA lectin receptors in human corneal epithelium. Use of cryosections may be preferable, especially when a negative reaction is obtained using paraffin sections. It has been shown that human corneal epithelium stains with Lotus tetragonolobus and Dolichos biflorus only if frozen sections are used. In recent years, paraffin sections have been used extensively with success in the study of lectin binding sites. Formalin fixation and paraffin embedding would not be expected to alter lectin binding sites chemically, because glycosidic bonds are stable at high temperatures (up to 100°C) and in organic solvents as long as pH is maintained close to 7.0. Differences in the lectin staining patterns of frozen and paraffin sections are probably related to differences in the solubility properties of various macromolecules. Lipid-like molecules are extracted in solvents used for deparaffinization, and are thus not expected to be retained. On the other hand, glycoproteins are often retained in the formalin-fixed paraffin sections.

Biotin-labeled lectins may prove to be valuable probes in the identification of specific glycoconjugate abnormalities in corneal disease. We have recently identified abnormal glycoconjugates in corneas of patients with macular dystrophy using the methodology described herein.12

Key words: lectin receptors, glycoconjugates, cornea, human, cat, rabbit

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References

An Improved Method For the Delivery of Artificial Tears
Using an Infusion Pump

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Patients with markedly decreased or absent tear duct production require the frequent instillation of artificial tear preparations. Through animal experiments, a new method has been developed for the continuous infusion of these solutions. In this procedure, the canalicular system is intubated with fenestrated silastic tubing, which is subcutaneously tunnelled and then attached to a miniaturized and computerized pumping device. This makes it possible for a predetermined volume of solution to be automatically and continuously delivered. Using this technique, artificial tear solution was instilled at a rate of 1.75 μl/min, a rate approximating the normal basic tear secretion rate (0.5–2.2 μl/min). This resulted in a 14% increase in tear flow from preoperative values. This represents a 74% increase in tear secretion rates for patients with keratoconjunctivitis sicca. None of the experimental animals developed subcutaneous infections, dacryocystitis, or corneal ulcers. By utilizing the normal anatomy of the lacrimal drainage system, this new technique: (1) does not compromise the conjunctival cul-de-sac or the salivary system, (2) avoids the inconvenience of previous external devices, and (3) allows for the automatic instillation of predetermined volumes of artificial tear solutions. Invest Ophthalmol Vis Sci 27:1284–1288, 1986

The major therapeutic modality for patients with greatly decreased or absent tear production is the frequent instillation of artificial tear preparations. In se-
vere cases, these preparations may be necessary every few minutes to achieve ocular comfort as well as therapeutic efficacy. In some cases, slowly released artificial tears\(^1\) and punctal occlusion\(^2\) have helped to reduce the frequency of tear replacement. Parotid duct transplantation represents a more radical approach to the treatment of dry eyes.\(^3\) We describe a new tube delivery system for the continuous infusion of artificial tear preparations that uses an indwelling fenestrated catheter and an automatic infusion pump.

**Materials and Methods.** Four mongrel dogs, weighing between 11–14 kg each, underwent placement of silastic tubing as described below. An automatic pump and 3 ml syringe device (AS6C Auto Syringe pump; Travenol Laboratories, Inc., Hooksett, NH) (Fig. 1) with a 24-inch microvolume intravenous set attached was taped to the dog's body. The intravenous infusion set was attached to the fenestrated silicone tubing by inserting the 27-gauge needle cemented to the end of the infusion set into the lumen of the silastic tubing. The Auto Syringe pump was set to deliver an artificial tear solution (Tears Naturale; Alcon Laboratories, Inc., Fort Worth, TX), at a rate of 1.75 \(\mu\)l/min or 2.52 ml/day. Since the pump contained a 3 ml syringe, daily refilling of the pump was required.

Flow of the artificial tear solution across the cornea was evaluated by placing several drops of 5% fluorescein sodium within the artificial tear solution. The tear flow was then evaluated with slit lamp biomicroscopy.

A modified Schirmer tear test was used to quantitate tear flow.\(^4\) Without local anesthesia, each of the dog's lower lids was retracted, and the bent end of a Schirmer tear test strip was placed over the lower eyelid margin for 1 min. During that time, the lids may be kept closed or open. The strip was then removed, and the amount of wetting was compared to the scale on the outside of the test strip package. The normal Schirmer value for a dog averages 20 ± 3 mm/min (10.9–14.9 \(\mu\)l/min).\(^4\) For each of the experimental animals, Schirmer tear testing was performed three times prior to the start of artificial tear infusion and three times during infusion. The authors of this manuscript adhere to the ARVO Resolution on the Use of Animals in Research.

The experiment was carried out for a period of 6 weeks, after which it was arbitrarily terminated. The animals were sacrificed 4 months following the end of the experiment. For logistical reasons, infusion of tears was continuously carried out for three 1-week periods within the 6 weeks of the experiment. Tear flow in ml/min was determined by converting the mm of Schirmer tear strip wetting using the nomogram developed by Lamberts et al.\(^5\)

**Surgical technique:** Each experimental animal was anesthetized with 20–25 mg/kg of intravenous thio- pental sodium. Following endotracheal intubations, the dogs were shaved, prepared, and draped for a standard dacryocystorhinostomy.

A No. 15 Bard-Parker blade was used to make a rectilinear skin incision 10–11 mm nasal to the medial canthus, beginning 1–2 mm above the medial canthal tendon and extending for approximately 20 mm in a direction perpendicular to the tendon. A Steven's scis-
Skin, fascia, angular vein and peristeme retracted

Anterior lacrimal crest

Double knot with retaining suture at end of tube

Lacrimal sac

Tube loop in place with knotted end drawn into lacrimal sac

Fig. 2. a, Intubation of canalicular system with fenestrated silicone tubing prior to fixation of tubing in lacrimal sac. b, Silicone tubing with lacrimal sac closed and fenestrations positioned between superior and inferior puncta. c, Subcutaneous tunnelling of silicone tubing. d, Silicone tubing in final position and attached to infusion pump.

Sors was used to dissect bluntly through the orbicularis muscle and expose the periosteum over the anterior lacrimal crest. When required, the angular vessels were ligated.

The periosteum was incised slightly nasal and parallel to the anterior lacrimal crest. A perioveal elevator was used to elevate the periosteum from the anterior lacrimal crest and the lacrimal sac from the lacrimal fossa. A No. 11 Bard-Parker blade and Wescott scissors were used to incise the lacrimal sac in a superior to inferior direction and to fashion anterior and posterior flaps.

The superior and inferior puncta were dilated with a lacrimal dilator. A canaliculus intubation set (Guibor Concept Canaliculus Intubation Set; Concept Co., Inc., Clearwater, FL) was used to intubate the superior and inferior canalicular system with silicone tubing. This intubation set consists of two stainless steel probes that are 17.7 cm long and 0.076 mm in diameter. Each end of a 29.21 cm length of silicone tubing (Dow Corning, Midland, MI) is cemented to the probes. The silicone tubing was modified by using a 27-gauge needle to create multiple fenestrations over a 1 cm length of the tubing 5 cm from one end (Fig. 2a).

Following intubation of the canalicular system, the stainless steel probes were removed, and the fenestrated portion of the tubing was positioned between the inferior and superior puncta (Fig. 2b). The short end of the silicone tubing was knotted and sutured into the lacrimal sac with a 4-0 Dacron suture (Fig. 3).

A No. 15 Bard-Parker blade was used to create a 2 mm vertical incision 15 mm lateral to the lateral canthus. The incision was carried down to the periosteum using Wescott scissors. A Wright ptosis needle was inserted through the incision and tunneled above the periosteum and below the inferior orbital rim to the area of the lacrimal sac. The free long end of the silicone tubing was then drawn back through this subcutaneous tunnel and pulled out of the lateral incision (Figs. 2c, d). A second 2 mm incision similar to the first was made posterior to the ear, and the Wright needle was again used to draw the silicone tubing subcutaneously and out of this incision. The silicone tubing was sutured to the skin behind the ear with 4-0 silk sutures.
The lacrimal sac flaps and periosteum were closed with 4-0 polyglactin 910 (Vicryl) sutures; the orbicularis was closed with 5-0 Vicryl sutures; and the skin was closed with 4-0 sutures. The 2 mm skin incisions were closed with 4-0 silk sutures.

**Results.** Table 1 summarizes the results of the Schirmer tear test for the four experimental animals. Prior to the start of tear infusion, the average Schirmer test strip wetting was 20.1 mm/min (12.9 μl/min). During infusion at a rate of 1.75 μl/min, average wetting increased by 2.8 mm/min to 22.9 mm/min (14.7 μl/min). This represents a flow change of 1.8 μl/mm, which is a 14% increase from the preinfusion rate. Evaluation of corneal wetting with slit lamp biomicroscopy showed regular wetting of the entire cornea between periods of eyelid closure during blinking.

None of the animals developed an ocular infection or corneal erosion during the period of the experiment or the four months prior to sacrifice. In addition, there were no cases of subcutaneous infection or dacryocystitis over this entire period. The fenestrated portion of the silastic tubing remained in good position through the entire experiment. In no case did any obstruction of the tubing develop and no flushing of the tubing was required at any time.

Two animals underwent removal and replacement of their indwelling silastic tubing to determine the ease with which this could be performed. In both cases, the previous surgical wound was easily opened to expose the tubing, which was then removed without difficulty from the sac, canalicular system, and subcutaneous tunnel. Replacement of the tubing was accomplished without difficulty or complication.

**Discussion.** Canalicular intubation with fenestrated silicone tubing attached to a miniaturized automatic pumping device offers a new approach to the control of tear deficiency states. A variety of other techniques for the continuous delivery of ocular solutions using tube delivery systems have been tried previously. These approaches have been inconvenient to use, irritating to the patient, and disruptive to the normal eyelid anatomy.

The technique described herein provides a new method for the delivery of artificial tear replacement in severe tear deficiency. The normal anatomy of the lacrimal drainage system is utilized to avoid compromising the eyelids or ocular fornices, which are important structures for the maintenance of an evenly distributed tear flow across the cornea.

The measurement of tear flow rates and volumes...
has been carried out by several researchers."\textsuperscript{5,10} Reflex tear flow rates have been measured to be 5.71 ± 5.86 \( \mu l/min\).\textsuperscript{10} Basic tear secretion ranges from 0.5–22 \( \mu l/min\), averaging approximately 1.2 \( \mu l/min\).\textsuperscript{5} Using the pumping device described in this report, artificial tears could be delivered at a rate of 1.75 \( \mu l/min\), or 2.52 ml/day, which is approximately the normal basic tear secretion rate. This rate of delivery was able to increase modified Schirmer tear test wetting in normal canines by 2.8 mm/min, which equals approximately 1.8 \( \mu l/min\) when converted to a flow rate using a standard nomogram.\textsuperscript{5} Reflex tear flow rates in patients with keratoconjunctivitis sicca are approximately 2.42 \( \mu l/min\) less than those of controls.\textsuperscript{10} This rate can be increased 74% through the use of the automatic tear delivery system described in this report, and may significantly improve the symptoms and decrease the corneal pathology of patients with severe deficiencies in tear production.

The canalicular system is intubated with silicone tubing during a variety of oculoplastic procedures, including dacryocystorhinostomy, repair of canalicular lacerations, and treatment of nasolacrimal duct obstructions without dacryocystorhinostomy.\textsuperscript{11} This tubing commonly remains in the canalicular system for long periods of time.\textsuperscript{11} While punctal erosion and tube migration are the most common complications associated with this device, these complications are rare and the silicone tubing is well tolerated in the canalicular system.\textsuperscript{11}

Subcutaneous silicone catheters are commonly used for the long-term delivery of chemotherapeutic agents and parenteral nutrition.\textsuperscript{12} While subcutaneous infections are a complication of these catheters, at least one study\textsuperscript{12} has reported no subcutaneous infections in catheters implanted for 1–2 yr in cancer patients receiving regular chemotherapy. No experimental animals in our study developed a subcutaneous infection; nonetheless, maintaining cleanliness at the skin entry site and sterility of the artificial tear solution are important in preventing infection. The use of a totally implantable pump system (Infusaid Corp., Norwood, MA) could be a method to avoid infectious agents entering the skin at the catheter exit site. However, since the silicone tubing was easily removed and replaced, this could be carried out in cases of subcutaneous infection that fail to respond to antibiotics and other therapies.

The technique of providing tear replacement solutions using a subcutaneously tunneled fenestrated silicone tube attached to a miniaturized infusion pump may be beneficial to patients with severe keratoconjunctivitis sicca. It may also prove useful to patients requiring ocular therapy for other conditions, such as glaucoma, or chronic uveitis. Further evaluation of this technique in patients with severe tear deficiency states, as well as other conditions, is needed to test its capabilities fully.

**Key words:** dry eyes, artificial tear infusion pump, keratoconjunctivitis sicca

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**References**


Anaphylatoxin Levels in Human Aqueous Humor

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Radioimmunoassay was used to measure levels of C3a, C4a, and C5a in aqueous humor from 13 normal eyes, 8 noninflamed eyes with a history of surgery or inflammation, and 14 eyes with anterior uveitis. The authors were unable to...