An implantable system is described which continuously delivers an aqueous solution to the external surface of six rabbit eyes for 6 weeks. A polytetrafluoroethylene (PTFE) tube was implanted in the superior conjunctival fornix 4 weeks prior to the implantation of the Infusaid pump. The pump provides a fluid source which is easily refilled and requires no batteries or external power source.

The continuous delivery of drugs to the ocular and periocular tissues is useful in pharmacological studies in rabbits. The recently developed Alzet osmotic minipumps are self-powered implantable pumps which deliver solutions of experimental agents to the rabbit eye at controlled rates for periods of up to 1 week. Experiments of longer duration require replacement of the minipumps, which entails a risk of inflammation and infection at the pump sites. We describe herein an implantable closed pump and tube system that has been devised for the continuous delivery of aqueous solutions to the external rabbit eye for at least 6 weeks.

Materials and methods. The pump used in this system is the Infusaid manufactured by Metal Bellows Corp. (Fig. 1). This pump was developed and is being used for long-term anticoagulation therapy. The pump is a two-chambered device, with one chamber containing the drug in aqueous solution and the other containing the charging fluid. The charging fluid is a fluorocarbon in liquid-gas equilibrium which is altered by body temperature. The driving force of the expanding charging fluid at body temperature and the fixed outflow resistance combine to provide a constant flow rate for an aqueous solution.

The pump currently available is the Model 100, which has a drug volume of 47 ml, a diameter of 86 mm, a thickness of 27 mm, an empty weight of 189 gm, and a rate of delivery of 1 ml/day. Small pumps, with a volume of 5 ml, are being developed. The smaller pumps should be better suited to animal experimentation than the larger models described in this paper.

An expanded polytetrafluoroethylene (PTFE) tube was designed in cooperation with Gore Associates for externalization of the system in the superior conjunctival fornix. The PTFE tube consists of an outer surface containing interspaces, which is compact enough to prevent further tissue ingrowth and occlusion of the lumen. Larger-diameter tubes of expanded PTFE have been used in vascular surgery for venous and arterial grafts.

The PTFE tube was implanted in the superior conjunctival fornix of six rabbits 4 weeks prior to the implantation of the pump. A location in the superior conjunctival fornix was chosen for insertion of a metal cannula. The cannula was directed subcutaneously from the superior fornix to an exit site over the occipital region. The PTFE tube was then withdrawn through the exit site, leaving the PTFE tube in place. The PTFE tube was sutured to the conjunctiva with 7.0 Prolene suture so that the external orifice was 1 to 2 mm beyond the plane of the conjunctiva. Previous experiments in which the external orifice of the PTFE tube was positioned more than 2 mm beyond the plane of the conjunctiva resulted in extrusions, whereas placement of the orifice in the plane of the conjunctiva resulted in retractions. The PTFE tube was then anchored posteriorly to the periosteum over the occipital region with 4.0 prolene. The exit site in the occipital region was also closed with 4.0 prolene. The tube was allowed to remain undisturbed for a period of 4 weeks prior to the implantation of the pump so that fibrous tissue ingrowth would secure the tube firmly to the surrounding tissues. Previous experiments in which the PTFE tube and pump were implanted simultaneously resulted in retraction or extrusion of the PTFE tubes in the superior conjunctival fornix.

The Infusaid pump was implanted in a subcutaneous pocket in the lumbar region of the six rabbits 4 weeks after placement of the PTFE tube. The silicone catheter attached to the outlet of the pump was passed subcutaneously and connected to the PTFE tube in the occipital region. The incision sites in both the occipital and lumbar regions were closed with 4.0 prolene suture.

It was necessary to refill the pump every 4 weeks. This was accomplished by passing a 22-gauge Huber point needle transcutaneously and piercing the inlet septum of the pump. Solution of filtered 0.9% sodium chloride and 0.5% fluores-
Fluorescein dye was added to the saline solution in order that flow to the eye could be monitored with a cobalt blue flashlight.

**Results.** A continuous flow to the external eye was maintained in the six adult rabbits for 6 weeks. The experiment was arbitrarily terminated at this point. The rabbits were observed at least three times each week for determination of the position of the tubes in the superior conjunctival fornix and detection of fluorescein in the eye. The orifices of the tubes were maintained 1 to 2 mm beyond the plane of the conjunctiva without significant retraction or extrusion (Fig. 2). The mild conjunctival hyperemia noted following implantation of the PTFE tubes in the superior conjunctival fornices disappeared in approximately 3 days. There were no external ocular infections in these six rabbits.
Discussion. The implantable system described in this report provides a method for delivering aqueous solutions to the external rabbit eye for at least 6 weeks. The PTFE tube is implanted in the superior conjunctival fornix 4 weeks prior to the implantation of the pump. During this time fibrous tissue ingrowth secures the tube firmly to the surrounding tissues. By allowing the tube to be anchored by fibrous tissue ingrowth, problems with extrusion or retraction are largely eliminated. The tube appears to be well tolerated, and the present system can be refilled repeatedly without surgical intervention or manipulation of the ocular tissues. This reduces the risk of inflammation and infection at the pump sites.


Key words: implantable, pump, continuous delivery, polytetrafluoroethylene tube, transconjunctival tube

REFERENCES


Mucus-stimulating factor in tears. RUDOLPH M. FRANKLIN AND BETSY G. BANG.*

Mechanisms responsible for regulation of tear film mucus are poorly understood. Humoral factors responsible for stimulation of mucus secretion can be studied in vitro by using the free-swimming urn cell, a normal component of the coelomic fluid of the marine invertebrate Sipunculus nudus. With this system, a tear mucus-stimulating factor was found in normal human tears but was markedly decreased in patients with dry eye syndromes. It is suggested that a mucus-stimulating factor exists in normal human tears and that a decrease in this substance may be instrumental in the pathophysiology of certain dry eye syndromes.

Abnormalities in mucus and its production are characteristic of various diseases, especially prominent in such conditions as cholera and mucoviscidosis. Endogenous mechanisms responsible for mucus stimulation are not well understood and could contribute to the pathogenesis of some diseases.1,2

In mammalian systems, goblet cells responsible for production of mucus along membranes may respond, at least in part, to nonneural factors.1 Evidence has been presented describing a polypeptide factor in patients with cystic fibrosis interfering with ciliary activity,3 which reflects alterations in the overlying mucus layer.4,5 Recently, a macromolecule has been found in the sera and secretions of patients with cystic fibrosis as well as in normal patients, capable of stimulating the urs system, a noninnervated mucus-secretory cell system.6 The present study examined the ability of this mucus-secretory cell system to detect mucus-secretory substances (MSSs) in tears and raises the question of the existence of regulatory factors for tear mucus production.

Methods. The assay system for MSS uses the