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 Infusaid pump provides a fluid source which is easily refilled and requires no batteries or external power source.

The system provides a convenient, dependable method for delivering drugs to the external eye for at least 6 weeks. This is an advantage over the Alzet minipump, which lasts for approximately 1 week and requires replacement thereafter. 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.

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

REFERENCES


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, which reflects alterations in the overlying mucus layer.3, 4 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 urn 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 raised the question of the existence of regulatory factors for tear mucus production.

Methods. The assay system for MSS uses the

April 1980
free-swimming urn cells from the coelomic fluid of
the marine invertebrate Sipunculus nudus. Briefly,
these scavenger cells function in vivo by produc-
ing long mucus tails in response to defined stimuli.
Foreign debris, pathogens, and dead cells become trapped and then excreted from the animal.

Urn cells are maintained in vitro in the superna-
tant fluid of S. nudus whole blood (coelomic fluid)
at 4°C. The test is performed by mixing 5 μl of
test substance and 5 μl of urn cell fluid (approxi-
mately 50 to 100 urn cells) in a depression slide at
22°C. If the test substance contains an MSS, a tail
of mucus is induced on the urn cells, and the
length of tails is measured with a micrometer eye
piece in a light microscope. The average length of
30 tails after a given time (usually 20 min) is ex-
pressed in multiples of the average length of the
urn cell vesicle (approximately 70 μm).

Tears were collected from 18 normal human
volunteers. A blunt end of a white blood cell dilut-
ing pipette was touched to the tear meniscus with-
out rubbing the conjunctiva, and 10 to 100 μl of
fluid were collected. No effort was made to induce
tear production. Nine patients with various "dry
eye" conditions were also examined. Samples
were stored at -70°C until tested.

A pool of normal tears was dialyzed in cello-
phane membranes against several changes of an
excess of filtered (Millipore filter, 0.45 μm) seawa-
ter. The retentate was then compared with the
starting pool in the urn cell assay.

Individual tear samples were heated in sealed
glass tubes to 85°C for 5 min in order to test
temperature sensitivity.

**Results.** All tear samples from normal individu-
als gave urn scores (tail lengths) between 4 and 6
(Table I). In some instances, samples were rerun
with similar results. All three groups of patients
with ocular disorders showed highly significant
lower levels of MSS activity when compared to
normals (Table I). The MSS from normal tears did
not dialyze through cellophane membranes after 5
days.

Tear samples from normal volunteers could be
titered to 1:32 before losing activity, and heating
at 85°C for 5 min did not destroy the stimulating
activity.

**Discussion.** The present study examined the
ability of human tears to stimulate an invertebrate
mucus-secreting cell. Previous studies demon-
strated the ability of the urn cell to respond to sera
and other biological fluids from patients with cystic
fibrosis as well as from normal subjects. The
present study again demonstrated the activity in
tears from normal patients to stimulate mucus
production by the urn cell and, in addition,
showed that patients with certain dry eye syn-
dromes have low levels of this activity.

Mucus represents a major component of normal
tears and acts as a wetting agent over the corneal
epithelial surface. Decreased goblet cell num-
bers, as well as diminished tear film stability, have
suggested that mucus deficiency might represent a
primary cause of ocular change. Whether such
primary disorders exist remains speculative, but
they could result from failure of a local stimulus to
the goblet cells.

The mechanism of control of mucus secretion in
ocular as well as nonocular structures is unclear
and may depend on both nervous and chemical
stimulation. A substance has been found in the
serum and in the medium from skin fibroblast cul-
tures from patients with cystic fibrosis. Its activity
is assayed by its effect on the movement of ciliated
epithelium from rabbit trachea and oyster gills,
which directly reflects changes in the overlying
mucus layer. Recently the urn cell assay has
demonstrated MSSs in sera and certain secretions
from patients with both cystic fibrosis and chol-
era. These early studies suggested that the
urn system offered a method capable of identifying
molecules responsible for regulation of mucus se-
cretory systems, unencumbered by the problems

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**Table I. Urn cell stimulation by lacrimal fluid**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Mean ± S.E.M. *</th>
<th>Range</th>
<th>P value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ocular pemphigoid (2)†</td>
<td>3.0 ± 0</td>
<td>3.0</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>Stevens-Johnson syndrome (3)</td>
<td>2.2 ± 0.5</td>
<td>1.4-3.0</td>
<td>&lt;0.002</td>
</tr>
<tr>
<td>Keratoconjunctivitis sicca (4)</td>
<td>2.3 ± 0.3</td>
<td>1.5-3.0</td>
<td>&lt;0.002</td>
</tr>
<tr>
<td>Normal (18)</td>
<td>5.2 ± 0.1</td>
<td>4.0-6.0</td>
<td></td>
</tr>
</tbody>
</table>

*See Methods for unit.
†vs. normal by Mann-Whitney U test, two tail.
†No. of patients in parentheses.
of the highly subjective bioassays previously employed.\textsuperscript{12}

That MSS in tears reflects part of a normal physiological mechanism is supported by an absence or low levels of this activity in patients with Stevens-Johnson syndrome and ocular pemphigoid—mucus deficiency diseases. Curiously, keratoconjunctivitis sicca patients, known to have primarily an aqueous tear-layer deficiency, also demonstrated low levels of MSS in their tears. It is possible that the activity originates with aqueous tear components in the lacrimal gland and remains at a constant concentration. Since the assay is performed at a constant tear volume, the amount of aqueous tear examined would be extremely low.

The tear substance responsible for the stimulation in this system could reside with any of the nondialyzable tear macromolecules. Whether the MSS activity resides with a previously described tear macromolecule must await separation of tear components and isolation of the active fraction.

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Key words: mucus, urchin cell, tears, invertebrate, secretion, ocular pemphigoid

References


Cone threshold vs. retinal eccentricity: changes with dark adaptation. BRUCE DRUM.

Detection threshold vs. retinal eccentricity functions measured during the cone plateau of the dark-adaptation curve differed from comparable functions measured on a uniform photopic background. Dark adaptation increased parafoveal sensitivity more than either foveal or peripheral sensitivity.

The variation of cone sensitivity over the visual field in the presence of a uniform photopic background is well known; sensitivity falls off rapidly in the parafovea from a sharp foveal peak, then declines more gradually toward the periphery. The slope of the eccentricity function is steeper for small targets than for large targets. Comparable cone data for dark-adapted conditions are difficult to obtain because the rods present in the extraofoveal retina are normally more sensitive. Because cones dark-adapt faster than rods, however, there is a period of several minutes after the extinction of a strong adapting light, known as the cone plateau, during which cones are completely dark-adapted but rods are still relatively insensitive.

Using a white circular test target with a 1° visual angle and a 1 sec duration, Sloan measured dark-adapted cone (DAC) thresholds during the cone plateau as a function of eccentricity and compared the results to a similar light-adapted cone (LAC) function for which the adapting luminance was 2.23 cd/m². The shapes of the LAC and DAC functions did not differ significantly for her single normal subject.