Treatment Of Dry Eye

Aghai GH. M.D
Iran University of Med. Science
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### Tear Film

**Physical Properties**
- 98% H₂O
- 6.9 μL volume
- pH 7.5
- 310-334 mOsm
- 6.5-7.5 μm thickness
- 12-16%/min turnover
- 0.06 μL/cm²/min evaporation
- 3.8 μL/min secretory rate

**Electrolytes (umol/L)**
- Na 120-160
- Cl 118-135
- HCO₃ 20-25
- K 20-42
- Mg 0.7-0.9
- Ca 0.5-1.1
- Gluc 0.5-0.7
- Retinol
- Urea

**Proteins**
- Lysosome
- Lactoferrin
- Lipocalin
- Albumin
- Orosomucoid
- IgA, IgG, IgM
- Polar phospholipid

**Enzymes/Inhibitors**
- Glycolytic
- Amylase
- Plasminogen activator
- α2-macroglobulin
- α1-antitrypsin
- Ceruloplasmin
- Albumin

**Tear Film Components**
- **Superficial Lipid Layer**: 0.1-0.2 μm thick
- **Aqueous Layer**: 7.8 μm thick
- **Adsorbed Mucin Layer**: Over 1 μm thick
- **Microvilli of Epithelium**: Extend into and stabilize mucin layer

**Additional Information**
- Lacrimal gland
- Goblet cells
- Meibomian glands
- Mucous layer
- Watery layer
- Ciliary layer
Dry Eye: Etiology

A) Tear Deficiency:

* Sjogren’s synd.
  primary
  secondary (Arthr. Rheum -lymphoma – sarcoidosis –……)

*non- Sjogren’s:
  lacrimal gland diseases

B) Evaporative loss:

  MGD
  lagophthalmos
  Etc; blinking disorders , C.L. , ……

Dry eye causes inflammation ,&
interrupts healthy ocular surface.
Dry Eye : treatment

Dry eye /ocular surface disorder is:
progressive, life-long, inflammatory, symptomatic disease.
Treatment must aim for:
* explanation of disease & psychotherapy
* prevention of aggregative factors,
* treatment of the cause (inflammation),
* stimulation of tear secretion,
* Replacement of tear,
* Maintenance of tear,
* treatment of ocular surface disorders,

present treatments are only palliative,
Although Dry eye isn’t curable,
But new trials are against the causes.
Dry Eye: prevention of aggregative factors

A medications (Atropines, anti-histaminic, Beta-blockers, contra-septives, diuretics, Retinoid, chemotherapy, anti-glaucoma, preservatives)

B environment (low humidity – dust – smoke – allergens – cosmetics) (≠ air conditioners - + humidifiers - + goggles ?)

C long periods of near work (computer -…) – overnight jobs

D viral inf. , allergy .

E pregnancy – Hormone replace therapy

F C.L.

G some ocular surgeries (refractive surgery – blepharoplasty keratoplasty - ECCE)

Exposure to a controlled adverse environment impairs the ocular surface of subjects with minimally symptomatic dry eye.


[Does the modern office environment desiccate the eyes?]

Dry Eye : lubricants
Replacement of tear

Artificial tear (drops - gel – pomade – spray – inserts-…)

Indications of use :

A) symptomatic relief of dry eye.
B) symptomatic relief of irritants (wind – sun -....)
C) symptomatic relief of exposure .
D) refreshment of contact lenses & prosthesis.
E) as basis for preparing topical medications .

( e.g. ; fort antibiotic drop)
<table>
<thead>
<tr>
<th>Component</th>
<th>Description</th>
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<tr>
<td>Solvent</td>
<td>(water)</td>
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<tr>
<td>Active ingredient</td>
<td>(water soluble polymers)</td>
</tr>
<tr>
<td>Viscosity</td>
<td>(polymers concentration)</td>
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<tr>
<td>Preservatives</td>
<td>(prevention of contamination)</td>
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<td>balanced tonicity</td>
<td>(Inorganic electrolytes)</td>
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<td></td>
<td>(NaCl &amp; KCL equivalent to 0.9% NaCl)</td>
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<tr>
<td>P.H</td>
<td>(buffers)</td>
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<tr>
<td>Anti-oxidants</td>
<td>(Sometimes Vit. A)</td>
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<tr>
<td>Lipids</td>
<td>(phospholipids)</td>
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Artificial Tear Eye drops

Active ingredient (water soluble polymers) provides viscosity & tear film stability

Hyaluronic acid
Cellulose & methylcellululose & their derivatives:
  - hydroxypropyl Cellulose
  - hydroxyethyl Cellulose
  - hydroxypropyl methylcellululose (HPMC) 0.2% & 0.3% & 0.5%
  - carboxymethylcellululose 0.25% & 0.5% & 1% Carmelosa (low viscosity)
Polyvinyl alcohol 1.4%
Povidine 0.6%
Glycerin 0.3% & 1%
dextran 70
propylene glycol (PG)
polyEthyleneGlycol (PEG 400)
polycarophil
hydroxypropyl Agar (Systane ®)
Artificial Tear Eye drops

Mechanisms of effect:
classical view of the tear film: a 10-micron film of aqueous tears, sandwiched between thin layers of lipid and mucous.
mucous promoting tear adherence.
lipid preventing evaporation & has been challenged recently that:
1) the tear film may be considerably thicker than 10 microns, &
2) dissolved mucus and protein may form a structured aqueous gel that adheres to the epithelium and covers its irregularities, thus providing a high-quality optical surface.

Artificial tear provides a viscous layer which:
Stabilize & thicken pre-corneal tear film.
prolongs tear film B.U.T.
keeps ocular surface wet & lubricated.
helps to repair ocular surface damage
keeps ocular surface smooth
(improves decreased vision & aberrations)

Changes in ocular aberrations after instillation of artificial tears in dry-eye patients.

Due to temporary effect of these drugs, Consider for other long term therapeutic options.
Artificial Tear Eye drops

Preservatives:

Benzalkanum chloride
(0.01% for eye-drops, 0.02% for C.L. solutions & 1% as disinfectant)

Chlorbutanol.

Chlorhexidine (0.002-0.005%)

Thimerosal & mercuric oxides (0.002-0.005%)

EDTA.

Methylparaben.

Propylparaben.

Polyquad (SPK)

Purite.

Potassium sorbate.

Sodium perborate (air touch changes to H2O2, then H2O & O2)

Sorbic acid (less toxic)
Artificial Tear Eye drops

Ocular complications of Preservatives:

- **pigmentation**  (mercury deposits in lids – conj. – cornea & lens)
- **iritation**  (redness – photophobia – lacrimation – burning –….)
- **allergic**  dermatitis & urticaria & eczema – blepharitis –
  papillary & follicular conjunctivitis – pseudo membrane
  pemphigoid – symblepharon
  SPK – corneal edema – panus – corneal opacity –
  adherence to CL. & CL. intolerance –
  ocular surface mal-function & inflammation
- **Toxic**  Epith. Cell exfoliation, SPK
  long term decreased tear

Due to side effects of preservatives, now **preservative – free** artificial tears are made, but most of them are in **unit dose** form (chance of contamination), Also they are expensive.
Artificial Tear Eye drops

Ocular complications of Preservatives:

there is gross surface abnormalities in dry eye syndr. including;
inflammation, goblet cells loss , squamos metaplasia & decreased cell functions.
Several physiologic & microscopic studies have shown:
non-preservative artificial tears improves either) cell functions or) symptoms.
Preservatives artificial tears improves symptoms but increase cell mal-functions & death.

Toxic effects includes epith. Cell wall destruction & microvilli loss &
Preservatives in particular may influence mucin adhesion and maintenance of a
continuous tear film (tear BUT)
Preservatives has no effect on lipid layer & tear film evaporation.

Long time & frequent use of eye- drops can cause allergy to preservatives
( which can be immunologic hyper- sensivity or Idiosyncratic hyper –reactivity )
These complications are often mild & temporary & superficial .
these are usually reversible after stopping drug.
### Ocular complications of preservatives: journal review

#### Allergic contact sensitivity to benzalkonium chloride: Cutaneous, ophthalmic, and general medical complications.

A physician developed a severe allergic conjunctivitis from an ophthalmic solution containing BAK and became worse with use of another preparation containing BAK. The patch test reaction to BAK was strongly positive.

#### Effect of preservatives in artificial tear solutions on tear film evaporation.

Relative costs of various preserved artificial tear solutions for the treatment of dry eye conditions.

#### The conjunctival epithelium in dry eye subtypes: effect of preserved and non-preserved topical treatments.

The conjunctival inflammation and reduced goblet cell density of dry eye is exacerbated by use of preserved topical agents, and is not significantly improved by use of non-preserved artificial tear supplements alone. Therapeutic strategies for dry eye should aim to increase goblet cells and control ocular surface inflammation.

#### Acute effects of Chlorbutanol- or Benzalkonium chloride-containing artificial tears on the surface features of rabbit corneal epithelial cells.

Twice-daily use of a Chlorbutanol-preserved artificial tear on rabbit corneal epithelium assessed by scanning electron microscopy.

Quantitative evaluation of the corneal epithelial barrier: effect of artificial tears and preservatives.

Cytotoxic effects of benzalkonium chloride and chlorobutanol on human corneal epithelial cells in vitro.

Preservative-free artificial tear preparations. Assessment of corneal epithelial toxic effects.

Effects of preservative-free artificial tear solutions on corneal epithelial structure and function.
Preservative – free artificial tears:

Usually are single – dose, sometimes multi-dose.

Bion tears (24 S.D)

Tears Natural free (32 S.D)  
ALCON

Dry Eye Therapy (3cc)

Moisture eyes preservative free (32 S.D)

Moisture eyes liquid gel preservative free (28S.D)

Occucoat PF (28S.D)  
B & L

Celluvisc (30 & 50 S.D)

Refresh (30 & 50 S.D)

Refresh Plus (30 & 50 S.D)

Refresh Endura (20 S.D)  
Allergan

Aquasite (24S.D) (6cc & 15cc)

GenTeal (36S.D)

Hypotears PF (30S.D)  
Novartis

Tears again MC (15cc)

Thera tears (32S.D) (15cc & 30 cc)

Vision

Viva drops (10cc & 15cc)  
Vision Pharma
Artificial Tear Eye drops

Dosage & frequency of use:
As frequent as needed:
Q 15min ~ occasionally if necessary

Some believe & advise for a scheduled regimen: (e.g. Q 6h)

Compliance with and typical usage of artificial tears in dry eye conditions.
Only 63% (114 of 229) of recommended patients continued to use it as: one or two drops per day (30 gtts/30 days, +/- 89). (a great deal of day-to-day variability is seen within any individual)
& only 47% (42 of 89) used recommended ointment.
Patients appear to titrate dosage to symptoms on any given day, so there may be little reason to prescribe a specific dosage regimen for the majority of persons using tears.

Ocular surface residence times of artificial tear solutions.
sodium hyaluronate solution had a mean half-life on the ocular surface of 321 s, significantly longer than hydroxypropylmethylcellulose (44 s; p = 0.012) and polyvinyl alcohol (39 s; p = 0.013).
Artificial Tear Eye drops

Storage:

- Keep out of the reach of children.
- Don’t keep outdated medicine.
- Keep away from direct light & air (air-tight bottles)
- Keep between 8°C ~ 35°C (room temperature)
  (no need for refrigerator) [Store away from heat (>40°C)]
- Care for bottle head contamination
  (≠ hand touch)  (close immediately after use)
- After opening, use in a maximum period of 15 - 30 days!
### Gel tears

- Less greasy than pomades.
- **Refresh liquigel**  
  (15 & 30 cc) (Allergan)
- **Gen teal gel**  
  (10cc) (Novartis)
- **Gen teal lubricant**  
  (10cc) (Novartis)
- **Tear again night & day**  
  (3.5 gr.) (occusoft)
- **Tear again preservative free**  
  (3.5 gr.) (occusoft)

#### Gel tears. A new medication for the treatment of dry eyes.


55 patients (106 eyes) with severe dry eyes, who were unable to obtain ocular comfort with frequent administration of a wide variety of commercially available artificial tear preparations, 78% were improved by Gel tear therapy. on a dose of once - twice daily

#### Corneal contact time of artificial tear solutions.


A new artificial polyacrylic-based tear gel (Vidisic, produced by Dr. Mann, Berlin) was compared with a well-known artificial polyvinyl alcohol-based tear solution. The Vidisic concentration remained in the corneal tear film 7 times longer than the substance it was compared with. It was found that tear secretion improved for 2-4 hours (Schirmer test) and the stability of the tear film (BUT) improved for about 6 hours with Vidisic.

#### Carbomer- versus cellulose-based artificial-tear formulations: morphologic and toxicologic effects on a corneal cell line.


In vitro study, Carboxymethylcellulose artificial tears are less toxic than carbomer gel formulations. Questions about benefits of high-viscosity gels in the treatment of dry-eye syndrome still remain.

#### Studies on gel tears


Blurring of vision to a tolerable extent was observed with both HPMC and Carbomer 940 gel tears. No inflammation or discomfort was observed with either of the formulations.

#### Efficacy, tolerability and comfort of a 0.3% hypromellose gel ophthalmic lubricant in the treatment of patients with moderate to severe dry eye syndrome.

Emollients: simple Eye pomades

Base: Lanolin, Petrolatum, mineral oil, Also electrolytes, usually no preservatives.

They form an oily layer on ocular surface Which disseminates by blinking.

They remain longer than drops.

They are used for:

- Sever dry eye,
- Exposure keratopathy,
- Night time use in dry eye.

Use 0.25 -0.50 inch /fornix.

It causes slight irritation & temporary blurred vision.

Don’t use it with C.L. & Don’t Use pomades before eye drops.

Dura tears natural
  tears natural PM
  Moisture eyes PM
  Dry eyes
  Lacri Lube NP
  Lacri Lube SOP
  Refresh PM
  Akwa tears
  Tears renewed
  Tears again

(3.5 gr.) (Alcon)
(3.5 gr.) (B & L)
(3.5 gr.) (B & L)
(0.7 gr.) (Allergan)
(0.7 & 3.5 & 7 gr.) (Allergan)
(3.5 gr.) (Allergan)
(3.5 gr.) (Akorn)
(3.5 gr.) (Akorn)
(3.5 gr.) (occiusoft)
**slow release lubricants : [Lacrisert]** (Merck) (60s with applicator)
each rod contains 5mg hydroxypropyl cellulose  (It is preservative free )
It imbibes water , swells ,dissolves.
effect begins after 1 h & remains for 14–24 h  **{So 1 insert / morning is enough for 1 day}**
It is inserted in lower fornix  .
[ education is necessary (either by doctor or written directory of drug package)]

Disadvantages :
More expensive . (~ 55 us$ / box = 1us $ / day)
Manual dexterity is needed .
Sometimes blurred vision due to thick tear film (use BSS or physiologic serum)
Dislocation into palpebral fissure & irritation (even loss)
Complications as:  eye redness or discomfort ; watering of eyes ;
photophobia; matting or stickiness of eyelashes; swelling of eyelids;
In one study it was more effective than Artificial Tear Eye drops both
subjective (symptoms relief ) & objective test (tear B.U.T.)
Medications for Dry Eye

artificial tear spray

Less chance of contamination.

Tears Again Liposome spray (10cc) ($15) (ocusoft)

Natures Tears Eye Mist (10cc) ($7) (all scripts)
mucolytics
N- acetylcysteine (mucomyst) & Bromhexin.

Propriety name:
[Brunac (bruschetini)]

Usually it’s prepared by:
- mixing 5cc N- acetylcysteine 20%+ 5cc artificial tear.
- Keeping at 2-8’ C, up to 1 months.
- It has a bad odor & sense of burning on instillation.
- It lyses filaments & debris & mucous plaques
  (mucous – epith. Cells – lipids & proteins)
- Esp.; used for sever dry eye -filamentary keratitis & alkali burn.

Comparison of local acetylcysteine and artificial tears in the management of dry eye syndrome.
18/30 (60%) patients reported reduction of subjective discomforts, 10/30 (33%) no change, and 2/33 (7%) more discomforts with acetylcysteine than with artificial tear therapy. (A statistically significant difference (p=0.05), but had no effect on the objective signs of dry eye syndrome.
Artificial Tear Eye drops - New ideas

Autologous serum (vit A , TGF β – EPGF -…)

Albumin

Retinoic acid (decrease keratinization)

Anti-oxidants (decrease toxic effect of preservatives)

Chitosan

Chitosan as tear substitute: a wetting agent endowed with antimicrobial efficacy.


Cystane® (Alcon) Hydroxypropyl guar (HP Guar) 0.18%

Acts as gel (molecular network adherent to hydrophobic surface).

Useful in wounds repair (ocular surface)

Perhaps complementary with CsA.

No irritation or burning on use.

(15 s # 9$)

Topical androgens:

It seems; low Androgens accelerates dry eye (in menopause, pregnancy, milking) (so does high estrogens, but progesterone has no effect)

It’s supposed that; low Androgens causes MGD, so Abnormal lipids cause Evaporative Dry Eye.

Combined esterified estrogen and methyltestosterone treatment for dry eye syndrome in postmenopausal women.


The most important cause of Evaporative Dry Eye is MGD.
The effect of autologous serum eyedrops in the treatment of severe dry eye disease: a prospective randomized case-control study.
Autologous serum eye drops were found effective in the treatment of severe dry eye disease, as evidenced by improvement of tear stability and ocular surface vital staining scores.

Autologous serum eye drops for ocular surface disorders.

[Treating severe dry eye syndromes with autologous serum]

Symptomatic dry eye treatment with autologous platelet-rich plasma.

Albumin rescues ocular epithelial cells from cell death in dry eye.

Albumin as a tear supplement in the treatment of severe dry eye.

Iodide iontophoresis (anti-oxidant) as a treatment for dry eye syndrome.
Pre-clinical investigation of the efficacy of an artificial tear solution containing hydroxypropyl-guar as a gelling agent.

An evaluation of tear film breakup time extension and ocular protection index scores among three marketed lubricant eye drops.
Systane Lubricant Eye Drops was more effective than (Refresh Tears)&(Refresh Endura) at prolonging TFBUT up to 20 & 30 minutes after instillation.

Effective treatment of a mouse model of Sjögren's syndrome with eyedrop administration of anti-CD4 monoclonal antibody.

Double-masked, placebo-controlled safety and efficacy trial of diquafosol tetrasodium (INS365) ophthalmic solution for the treatment of dry eye.

Effect of an oil-in-water emulsion on the tear physiology of patients with mild to moderate dry eye.

Comparison of the efficacy of two lipid emulsion eyedrops in increasing tear film lipid layer thickness.

[Comparative study of treatment of the dry eye syndrome due to disturbances of the tear film lipid layer with lipid-containing tear substitutes]
Dry Eye: stimulation of tear secretion

**Secretagogues** (cholinergic agonists & Muscarinic) purinergic receptor (p2y2) agonist [Diquafosal (Inspire)]

stimulates mucin & tear secretion of Goblet cells.

Ocular allergy and dry eye syndrome.


**Oral Pilocarpine (Salagan)** (effective for dry mouth *not* dry eye)

(5mg tab x 4-6/day)

Successful Treatment of Dry Mouth and Dry Eye Symptoms in Sjögren's Syndrome Patients With Oral Pilocarpine: A Randomized, Placebo-Controlled, Dose-Adjustment Study.


**IBMX** (isobutyl-methyl xanthin)

**Eledoisin** (endekapeptides)
Dry Eye: treatment of the cause

A) MGD – allergy –

B) Lagophthalmos & exposure

C) ocular surface disorders
   proptosis – retraction – Ectropion – trichiasis – pterigium –

D) inflammation:
   ✓ systemic treatment of rheumatoid & other causes of Sjogren’s synd.
   ✓ topical anti-inflammatory drugs:

   recent clinical trials demonstrated effectiveness of topical Cyclosporin A 0.05%
The comparison of efficacies of topical corticosteroids and nonsteroidal anti-inflammatory drops on dry eye patients: a clinical and immunocytochemical study.


2 weeks Prednisolone eye drop {non-preserved Lotemax (Loteprednol Etabonate)] (20 s # 140$) decreased inflammation & dry eye symptoms & artificial tear need up to 3 months, Compared to (NSAIDS) or (artificial tear)
But due to side effects of corticosteroids ,it is only advised as acute course (2 weeks)

Effect of anti-inflammatory therapy on the treatment of dry eye syndrome]


short-term corticosteroids, cyclosporine A emulsion, oral tetracycline therapy, oral omega-3 fatty acid supplements, and autologous serum eye drops

A clinical study of the efficacy of topical corticosteroids on dry eye.


30 patients with mod. or severe dry eye, who were not sensitive to artificial tears, were treated with 0.1% fluorometholone eye drops. After 1 week of treatment, subjective symptoms were improved in all dry eye patients; objective tests were improved in all dry eye patients 1 month after treatment, and the difference was significant.
DRY EYE : RESTASIS® (CSA 0.05%)

**Active:** cyclosporine 0.05% (CSA) . **single use vials of 0.4 mL x 32 vials (90-150$)**

**Inactives:** glycerin; castor oil; polysorbate 80; carbomer 1342; water and sodium hydroxide to adjust the P.H

Its clinical benefits become apparent after about 3 months of therapy (1 drop X BID)

RESTASIS® : is an immune-modulator used for prevention of organ – transplantation rejection, It suppresses inflammation (lymphocytes infiltration – cytokines release – epith. Cells apoptosis -…)

Mechanisms of effect in dry eye isn’t clear.

RESTASIS® (phase 3 trial FDA approval 2002) showed statistically significant increases in Schirmer wetting of 10 mm at six months (5% of controls (vehicle treated) vs. 15% of RESTASIS® cases of dry eye patients whose tear production was presumed to be suppressed due to ocular inflammation.

Increased tear production was not seen in patients currently taking topical anti-inflammatory drugs, or using Punctal plugs.

**Contraindications:** RESTASIS® is contraindicated in patients with active ocular infections.

It hasn’t been studied in patients with a history of herpes keratitis.

**Adverse Reactions:** The most common adverse event of RESTASIS® was ocular burning (17%) after topical administration of RESTASIS® 0.05%, BID, in humans for up to 12 months, were below the quantitation limit of 0.1 ng / mL. There was no detectable drug accumulation in blood.

No effect on VA , IOP or cornea . (≠ corticosteroids)

**Conclusion:** it’s an expensive drug that may be effective in a small % of mod – sever KCS patients.
RESTASIS® JOURNAL REVIEW

An evaluation of the efficacy of a cyclosporine-based dry eye therapy when used with marketed artificial tears as supportive therapy in dry eye. Sall KN, *Eye Contact Lens.* 2006 Jan;32(1):21-6. (Cystne + Restasis) is more effective than (Cystane alone), or (Refresh + Restesis).


Phase III safety evaluation of cyclosporine 0.1% ophthalmic emulsion administered twice daily to dry eye disease patients for up to 3 years. Barber LD, *Ophthalmology.* 2005 Oct;112(10):1790-4. Therapy of chronic dry eye disease with cyclosporine 0.1% ophthalmic emulsion for 1 to 3 years was safe, well tolerated, and not associated with systemic side effects.


Dry Eye: treatment options

Usually treatment depends on severity of symptoms:

**Mild symptoms:**
- explanation of chronicity & need for long F/U
- preventive care
- treatment of MGD

**In mild ~ moderate symptoms:**
- above + artificial tear (PRN ~ QID)

**In moderate ~ severe symptoms (needs > than 4/day drops):**
- preservative –free artificial tear
- Lacrisert
- mucolytics
- CsA (Restasis)
- punctom plugs
- Tarsorrhaphy

**Sever cases** {ocular surface pathology (sterile or infectious)}
- above +
- low water content CL
- conj flap

........................
Dry Eye: surgical treatment

Usually when medications doesn’t alleviate symptoms.

Prevention of tear drainage (surgical Punctal occlusion)

Prevention of tear evaporation Tarsorrhaphy & cantorhaphy

Transplantation of secretory glands
Dry Eye: maintenance of tear

Prevention of tear drainage (surgical Punctal occlusion)

Temporary (absorbable collagen inj. & plugs –Gelatin)
( N-buthyl cyanoacrylate up to 2.5 w)

Reversible (Silicon – acrylamide & smart plug)

Permanent (thermal & electro-cautery –laser)
( conj. Graft)

Usually at first, temporary collagen plugs of only lower punctom;
If suitable (≠ over or undercorrection), then permanent plugs.
If there is reflex tearing, only lower punctom, otherwise both punctoms.
If still inadequate, then cantorhaphy.
soluble collagen inserts may be useful in treating dry eye syndrome. Statistically significant improvement in symptomatology and reduced necessity for artificial tears. But no significant change in rose Bengal staining or impression cytology results. (The absence of objective findings suggests the possibility of a placebo effect.)


Usually they are used for trial assessment of permanent punctal occlusion. Their effect lasts up to 3-14 days.

Tears natural RX
Tears savor RX
Collagen implant RX
Soft plug RX
Temporary punctal / canalicular Collagen implant RX

(60s 0.2, 0.3, 0.4, 0.5, 0.6mm) (Alcon)
(0.2, 0.3, 0.4, 0.5, 0.6mm) (Ciba vision)
(72s 0.2, 0.3, 0.4, 0.5, 0.6mm) (lacri Medics)
(60s 0.2, 0.3, 0.4, 0.5, 0.6mm) (oasis)
(72s 0.2, 0.3, 0.4, 0.5, 0.6mm) (Eagle vision)
Atelocollagen punctal occlusion in dry eye patients.
Atelocollagen punctal occlusion improves ocular surface disorders in dry eye patients.

Lacrimal duct occlusion for the treatment of dry eye.
Atelocollagen punctal occlusion
Silicon plugs: remains in place, but can be removed (reversible)

Complications:
- Irritation (erosions - GPC - allergic dermatitis - symblepharon -..)
- Pyogenic granuloma
- Adherence of bacteria to plug & infection
- Extrusion
- Migration into canaliculs (canaliculitis – dacryocystitis)

Usually 3 sizes (S – M – L)
Silicon plugs: Journal review


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<th>Manufacturer</th>
<th>Name/Description/Position</th>
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<tr>
<td><strong>Short-term occlusion therapy (less than 1 month)—Dissolvable intracanalicular collagen plugs</strong></td>
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<tr>
<td>Alcon, Ft Worth, TX</td>
<td>Tears Naturale™ Collagen Punctal Plug, vertical canaliculus</td>
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<tr>
<td>Eagle Vision, Marshfield Hills, MA</td>
<td>Temporary Collagen Plugs, 35 days, vertical canaliculus</td>
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<tr>
<td>Lacrimec Medical, Orcas Island, WA</td>
<td>Collagen Shorts, 3-5 days, vertical canaliculus</td>
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<tr>
<td>Oasis Medical, Glendora, CA</td>
<td>Collagen Plugs for the Lacrimal Efficiency Test, 4-7 days, horizontal canaliculus</td>
</tr>
<tr>
<td>Odyssey Medical, Memphis, TN</td>
<td>Soft Plug™ Collagen Absorbable, 2-5 days, vertical canaliculus</td>
</tr>
<tr>
<td>Surgical Specialties, Reading, PA</td>
<td>Collagen insert, 5-7 days, horizontal canaliculus</td>
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<tr>
<td></td>
<td>UltraPlug® Collagen Absorbable Punctal Plug, 3-5 days, vertical canaliculus</td>
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<tr>
<td><strong>Medium-term occlusion therapy (1-6 months)—Dissolvable intracanalicular synthetic plugs</strong></td>
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<tr>
<td>Lacrimec Medical, Orcas Island, WA</td>
<td>Dissolvable OPAQUE Herrick Lacrimal Plug®, about 6 months, horizontal canaliculus</td>
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<tr>
<td>Oasis Medical, Glendora, CA</td>
<td>Soft Plug Extended Duration Absorbable, up to 3 months, vertical canaliculus</td>
</tr>
<tr>
<td>Odyssey Medical, Memphis, TN</td>
<td>Extend™, up to 3 months, vertical canaliculus</td>
</tr>
<tr>
<td>Surgical Specialties, Reading, PA</td>
<td>Ultraplug® Extended Wear Synthetic, up to 2-6 months, vertical canaliculus</td>
</tr>
<tr>
<td><strong>Long-term occlusion therapy (more than 6 months)—Non-dissolvable punctum and intracanalicular plugs</strong></td>
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<tr>
<td>Alcon, Ft Worth, TX</td>
<td>Tears Naturale™ Punctal Plug, silicone, partially exposed at the punctum, full occlusion</td>
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<tr>
<td>Eagle Vision, Memphis, TN</td>
<td>SuperFlex™ Punctum Plug, silicone, partially exposed at the punctum, full occlusion</td>
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<td>FlexPlug® silicone, partially exposed at the punctum, full occlusion</td>
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<td>EaglePlug®, silicone, partially exposed at the punctum, full occlusion</td>
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<tr>
<td>FCI Ophthalmic, Marshfield Hills, MA</td>
<td>Flow Controller Punctum Plug, silicone, partially exposed at the punctum, full occlusion</td>
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<td>Ready Set™ Punctum Plug, silicone, partially exposed at the punctum, full occlusion</td>
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<tr>
<td></td>
<td>Slim Plug™, silicone, partially exposed at the punctum, full occlusion</td>
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</tbody>
</table>

Manufacturer Name/Description/Position

Locrimecics, Eastsound, WA
- PVP Perforated Plugs, silicone, partially exposed at the punctum, partial occlusion
- Blue OPAQUE Herrick Lacrimal Plug®, silicone, horizontal canaliculus, partial occlusion

Medennium, Travne, CA
- SmartPLUG™, thermosensitive hydrophobic acrylic, vertical canaliculus, full occlusion

Oasis Medical, Glendera, CA
- Soft Plug, silicone, partially exposed at the punctum, full occlusion
- Foam Fit Hydrogel, lower vertical punctum, full occlusion

Odyssey Medical, Memphis, TN
- Parasol® Punctal Plug, silicone, partially exposed at the punctum, full occlusion

Surgical Specialties, Reading, PA
- Ultraplug® Silicone Punctum Plug, partially exposed at the punctum, full occlusion

U.S. IOL, Laxington, KY
- OccuFlo™ Punctum Plug, silicone, partially exposed at the punctum, full occlusion

Tear Saver®, Tear Saver Plus®, and Tear Saver Collagen Inserts®, previously manufactured by Ciba Vision, are now the property of IOLTECH, France, and will be marketed in the USA by that company.
Smart plugs (thermo-sensitive acrylic)
Medeium (55 $)
Best performance under:
SLE (Magnification & illumination)
Cold light
Topical anesthesia
Needs a punctum dilator & forceps
Smart plugs: journal review

SmartPlug in the management of severe dry eye syndrome.
(55 eyes, 60.4%) reported a decreased use of lubricant eye drops after SmartPlug insertion, including 9 patients (14 eyes, 15.4%) who were free of supplementary lubricant eye drops. Forty-one patients (69 eyes, 75.8%) reported subjective symptom improvement after SmartPlug insertion. Complications included canaliculitis (6 eyes, 6.6%), epiphora requiring plug removal (5 eyes, 5.5%), and spontaneous plug loss (2 eyes, 2.2%)

Clinical evaluation of the Smart Plug in the treatment of dry eyes.


Canaliculitis, acute dacryocystitis, and tearing may be seen in patients who have had SmartPlugs. A trial of topical and oral broad-spectrum antibiotics followed by retrograde massage of the plug through the canaliculus may be helpful. If conservative measures fail, canaliculotomy with removal of the plug may be considered; DCR may be necessary. Although lacrimal irrigation may resolve the problem, irrigation also may dislodge the plug from its canicular position and cause permanent obstruction of the lacrimal drainage system.

Incomplete extrusion of an acrylic punctum plug in a case of severe dry eye syndrome.

[Pyogenic granuloma following Smart Plug insertion]

Pyogenic granuloma formation following placement of the Medennium SmartPLUG punctum plug.
Permanent Punctal occlusion:

In mild cases can cause epiphorea, in severe KCS has no effect (there is no tear), so it’s contra-indicated if:

- Schirmer >10mm
- Normal cornea
- Temporary conditions

Laser (Argon 50µ x 2” x 350-500mw) (after 30w recurrence 70%)

thermal & electro-cautery (superficial - deep) (after 30w recurrence 60% & 40%)

Surgical ablation (vert. canalicul curettage & suturing – Extirpation & cutting punctoms canaliculotomy & intra canalicul cautery outward subcutaneous displacement of punctoms

Removal of the vertical portion of the lacrimal canaliculus in dry eye syndrome]


Punctal Conj. Graft (reversible)
Tarsorrhaphy & cantorhaphy

Prevention of tear evaporation (decreased ocular surface)

Usually when corneal abnormality

Lateral – medial or both

Med cantorhaphy can be combined with incision & suturing of punctoms.

[Tarsorrhaphy: applications in a Cornea Service]
Dry Eye: surgical treatment

Transplantation of secretory glands:

A  conj. (only in unilateral trauma & burn)

B  mucosa (nasal – lip – maxillary sinus)

C  amniotic membrane

D  salivary glands:

  minor (with free lip mucosa in anophthalmic socket)

  free sublingual (usually necrosis)

  Parotid duct
    {epiphora of salivary tear (only water, no mucin or lipid)}
    (may cause microcystic corneal edema due to hypo-osmolarity)

  submandibular (in Temporal fossa, with anastomosis of it’s duct into conj. & temporal vessels anastomosis)
Submandibular gland transplantation

Lacrimation at first 2 weeks,
then Dry eye up to 3 months (innervations cut),
Re- lacrimation after 1 year {Salivary tear (mostly water, little mucous)}

management of lacrimation:
Medication. (parasympathetolytics)
BTA injection.
re-surgery (debulking)

Today this procedure is indicated for symptoms relief, not V.A improvement
{In severe end-stage Dry eye (Schirmer < 2mm, vascularized cornea)}
Dry eye treatment- New ideas & aims

A more effective polymers
B new harmless preservatives
C new anti-inflammatory agents
D topical androgens
E Secretagogues
از توجه و حوصله شما متشکرم.
Character of ocular surface mucins and their alteration in dry eye disease.  
Gipson IK, Hori Y, Argüeso P.  
Schepens Eye Research Institute and Department of Ophthalmology,  
Harvard Medical School, Boston, Massachusetts 02114, USA.  
Gipson@vision.eri.harvard.edu

At the ocular surface, three types of mucins are present. The large gel-forming mucin MUC5AC is expressed by conjunctival goblet cells. Some cells of the lacrimal gland acini express the small soluble mucin MUC7. The corneal and conjunctival epithelia express the membrane-associated mucins MUCs 1, 4, and 16. With the characterization of the mucin gene repertoire of the ocular surface epithelia, studies of the function of specific mucins, their gene regulation, and their alteration in ocular surface disease have begun. Current information suggests that all the mucins are hydrophilic and play a role in maintenance of water on the surface of the eye. The large secreted mucins represent the "janitorial service" that moves over the surface of the eye to wrap up and remove debris. The membrane-associated mucins form the glycocalyx, which provides a continuous barrier across the surface of the eye that prevents pathogen penetrance and has signaling capabilities that influence epithelial activity. Factors regulating mucin gene expression include retinoic acid, serum, and dexamethasone. Alteration in both secreted and membrane-associated mucins occur in drying ocular surface diseases. In Sjogren syndrome, MUC5AC expression is reduced, and in non-Sjogren dry eye, glycosylation of MUC16 appears to be altered. The pattern of expression of enzymes that glycosylate mucins is altered in ocular cicatricial pemphigoid. Therapies being evaluated for dry eye, including cyclosporine A, P2Y2 agonists, gefarnate, 15-(S)-HETE, and corticosteroids, may be efficacious due to their effect on mucin gene expression and secretion.