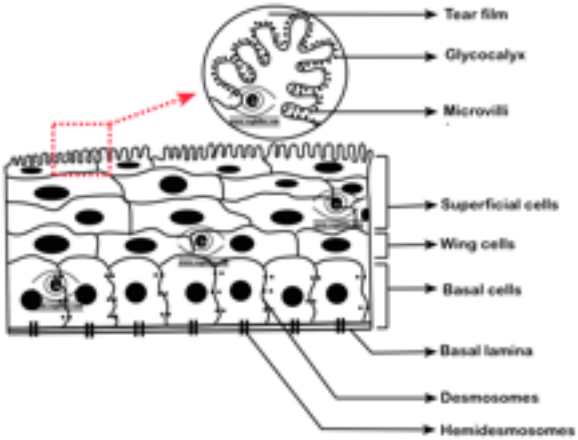
A STEPWISE APPROACH TO DRY EYES

Dr. Sameera Irfan, FRCS, Lahore, Pakistan.

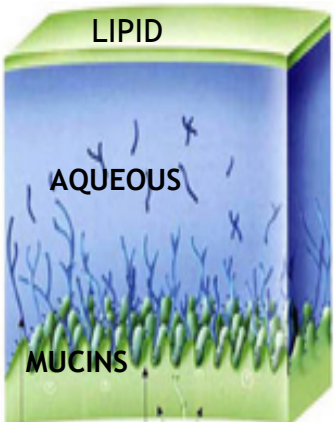
ITS A VERY COMMON PROBLEM, as It is a part of the normal AGEING process.



CORNEA IS A HYDROPHOBIC STRUCTURE & ACTS AS A SMOOTH POLISHED SURFACE BY VIRTUE OF A HEALTHY TEAR FILM. It is the Tear Film that makes it Hydrophilic.

Structure of corneal epithelium: It is thick peripherally towards the limbus but thins out towards the centre of the cornea. It is made up of basal columner cells that are adherent to the underlying Bowman's membrane via tight junctions, called Hemi-desmosomes: these junctions keep the corneal epithelium strongly anchored to the underlying stroma. Above the columner cells, are 2-3 layers of polygonal cells, called wing cells; above these are 3-4 layers of squamous epithelial cells, non-keratinized, and are tightly packed, with interdigitating adjacent edges, joined to each other by tight junctions called DESMOSOMES. This rigid structure acts like a strong brick-wall in which individual bricks are held together by strong cement (Desmosomes). This rigid structure prevents the water in the tear film and limbal blood vessels from penetrating the epithelium, keeping cornea a Hydrophobic and an avascular structure.

The cell membrane of surface epithelial cells, called apical cells, have numerous micro-villie to increase the surface area of corneal epithelium. To these microvilli, mucins, produced by the conjunctival goblet cells, adhere by covalent bonds and allows the aqueous component of the tear film to spread and attach to the cornea, thus making it a HYDROPHILIC STRUCTURE.



The layers of the epithelium are constantly undergoing mitosis. Basal and wing cells migrate to the anterior of the cornea, while squamous cells age and slough off into the tear film.

Three Layers of a Tear Film

- **Superficial lipid layer :** meibomian gland secretion. It Reduces tear film evaporation. It lubricates the ocular surface and the eyelids,

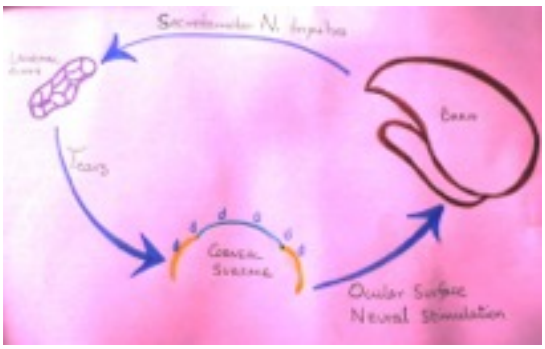
thereby allowing a smooth movement of the upper lid downwards over the cornea, spreading the tear film uniformly over the ocular surface and polishing the corneal surface. It also prevents bacterial adherence on the corneal surface.

- **Central aqueous layer:** isotonic tears secreted by the lacrimal gland (reflex secretion) & Accessory Lacrimal glands (basic tear production). It supplies oxygen, nutrients and epithelial growth factors to the cornea, polishes the cornea and is antibacterial because of the presence of immunoglobulins, isozymes, lactoferrin.
- **Inner mucin layer**: This is the most important layer being produced by the goblet cells present in the conjunctival and corneal surface epithelium. Normally corneal epithelium is Hydrophobic. Mucins cover the corneal epithelium and make it Hydrophilic so that the aqueous layer can stabilise over it and wet the corneal epithelium. They also freely float in the tear film, act as clean-up proteins, removing debris and bacteria.

Some Basic Facts: Dry Eye is a multifactorial disease; since there **are three layers of the tear film, so three main etiologic** causes should be looked for in every patient.

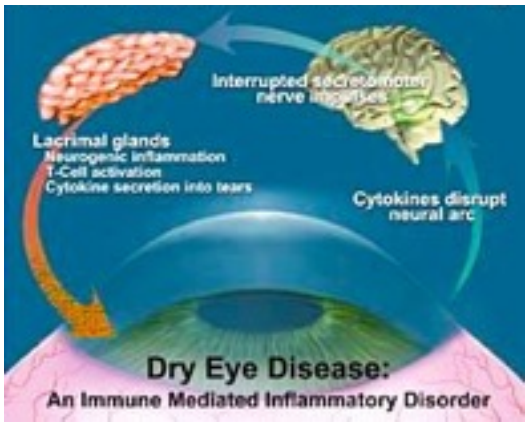
- Whether it is due to **reduced production** of aqueous component, resulting in increased tear osmolarity & chemical inflammation of the ocular surface.
- Or it is due to **increased evaporation** of aqueous due to deficiency of lipid layer.
- Or **poor wetting of ocular surface** due to mucin deficiency so aqueous layer is unable to wet the cornea, causing a dry, damaged hydrophobic corneal epithelium even in the presence of adequate tear production.
- Or it is due to a combination of all these factors, end result being HYPER-OSMOLAR TEARS CAUSING A CHEMICAL INFLAMMATION OF THE OCULAR SURFACE

Concept of LFU: Lacrimal Functional Unit



The aqueous component of tear film is produced by the lacrimal and accessory lacrimal glands in response to impulses travelling from the ocular surface (dried cornea/conjunctiva) to the brain. If the ocular surface is inflamed and damaged, less impulses will go the brain and tear production is reduced. Surface epithelial

cells sense the hyperosmolar environment and release inflammatory mediators, which cause cellular damage to the ocular surface, triggering heightened immune system activity. Less production of the aqueous component results in more hyper-osmolar tears and more inflammation of ocular surface, resulting in a vicious circle.



Symptoms: patients usually complain of Burning, Blurring of vision, glare while driving at night, Photophobia, too much tearing, paradoxically. All symptoms are worsened by smoking, reading, computer work, **chronically irritable eyes. When you see such a patient, you need to find answers to the following questions:**

1: IS THIS A DRY EYES SYNDROME ???
2: HOW WILL I DIAGNOSE IT ??
3: WHY IN THIS PATIENT: WHAT IS THE EXACT CAUSE ??
4: ARE THERE ANY PRECIPITATING FACTORS ? AGGRAVATING FACTORS ??
5: WHAT TESTS SHOULD BE DONE??
6: MANAGEMENT APPROACH : GRADING of Dry eyes & A STEP-WISE PLAN.

Pre-disposing Factors for a Dry eye: In addition to searching for a cause of the Dry eye, identify the pre-disposing factors which have aggravated the condition. Remember the term CLIDE, which describes two issues.

The first is for the condition known as Contact Lens Induced Dry Eyes, and the second is for the causes of dry eye: Climate, Drugs, Environment. The acronym becomes a handy tool when we understand the causes of dry eye.

1: Climate: dry, dusty, windy and cold climates.

2: Drugs: antihistamines, antidepressants, antihypertensives which are frequently diuretics, Parkinson's medications and oral contraceptives (by reducing androgen levels) can include dry eye as a side effect. beta blockers. antihistamines, AntiGlaucoma Therapy particularly Prostaglandin analogues: they damage goblet cells and stimulate Cytokine production. Preservatives in all these eyedrops damage tight junctions of corneal epithelium as well as damage conjunctival epithelium, goblet cells.

3: Environments : with dry heat or air conditioning can contribute to dry eye.
4: Insufficient blinking as can occur with computer use, long-term contact lens wear, eyelid disease, tear deficiency, ageing, menopause and diseases such as lupus, rheumatoid arthritis, ocular rosacea and Sjögren's syndrome.

5: Old age: Ageing causes androgen deficiency. Estrogen & androgen receptors are present in the lacrimal & meibomian glands. Androgens are trophic for these glands and are potent anti-inflammatory agents by producing (TGF beta) & suppressing lymphocytic infiltration of lacrimal glands. Androgen deficiency causes inflamed lacrimal and meibomian glands, with tear deficiency & hyperosmolar tears. These cause a pro-inflammatory environment on the ocular surface. Also cytokine production and T-cell activation further inflames ocular surface, disrupts the neural arc, Cytokines inhibit neuronal function and further convert androgens to estrogens by increasing the level of tissue degrading enzymes.

6: Connective tissue disorders: Rheumatoid arthritis, SLE.

7**: LASIK:** the cut flap destroys corneal nerves and disrupts the LFU permanently.

8**: Diabetes:** microangiopathy reduces blood supply to all glands; advanced glycation products in the tear film makes it hyperosmoler and promotes ocular surface inflammation. Autonomic neuropathy associated with type 2 Diabetes reduces the sensitivity of LFU.

9**: Vitamin A deficiency**

Examination:

1**:** Identify **the cause** as well as the **predisposing/aggravating factors** as both need to be treated. Look for blepharitis, Trachoma, Trichiasis, distichiasis, lower or upper lid entropion, lower lid ectropion, facial palsy, broken/loose corneal sutures, conjunctival scarring, corneal sensations

2: **Grade the severity** of Dry Eye prior to starting any therapy so that the efficacy of treatment given can be monitored. Inferior limbal punctate corneal staining is due to toxic meibomian secretions irritating the inferior conjunctival and corneal epithelium. A central corneal staining is due to evaporative tear loss and dryness of central corneal epithelium.

3: Examining the Tear Meniscus: The tear meniscus is a thin strip of tear fluid at the upper and lower lid margins. A low or absent meniscus is an indication of dry eye.

4: Tear film B.U.T. (Break Up Time) test evaluates tear quality, particularly mucin and meibum production, by measuring how long it takes for dry spots (or dark areas on a greenish film of Fluorescein-stained tears) to appear on the cornea after a blink. Normal is > 10 sec.

5: Schirmer's 2 Test: to measure basal secretion of tears, by anaesthetising the ocular surface with local anaesthetic eyedrops, and then placing a Schirmer's strip at the lateral half of the lid margin, while patient is looking above at the ceiling. He then closes his eyes and the reading is taken after 5 minutes, by observing how much of the filter paper became wet through capillary action. 15 mm or more is considered normal, nine to 14 mm indicates mild insufficiency, 4-8 mm indicates moderate insufficiency, and less than 4 mm indicates a severe aqueous deficiency.

Grading of Dry Eyes: This should be done at the first consultation in order to decide what kind of therapy the patient needs and monitor patient's improvement at each follow-up visit.

Levels	**1**	**2**	**3**	**4**
Visual symptoms	mild	moderate	severe	severe
Discomfort	mild	annoying	constant	constant
Conj. injection	none	none	+	++
Conj. Staining	none	moderate	++	+++
Corneal Staining	none	none	central	central
MGD	none	mild	Frequent	scarring
Tear Film BUT	> 10 mm	< 10 mm	< 5 mm	< 2 mm
Schirmers Test	> 10 mm	<10 mm	< 5 mm	< 2 mm

MGD= Meibomian gland Dysfunction: foaming over lid margins, capping of meibomian orifices, notching of lid margin where meibomian glands are absent due to scarred orifices.

Treatment Strategy:

LEVEL 1:

1: **Find the cause & Eliminate it. Look for pre-disposing factors.**

2: **Eyelid therapy**: scrubbing lid margin with a mild baby shampoo, tetracycline eye ointment massage onto the lid margin, hot fomentation of lid margins to melt fatty plugs on meiboman gland orifices, squeezing the fatty plugs out with upwards lid massage. Treat Trachoma by Tab. Azithromycin 1 Gm stat.

3: **Environmental & dietary modification**: Omega 3 fatty acids, Avoid air blowing in the eyes: hair dryers, car heaters, air conditioners, fans, add moisture to the air: a humidifier. Consider wearing wraparound glasses or eyeglass shields to avoid dry air, wind. Take eye breaks during long tasks: to evenly spread tear-film. Position the computer screen below eye level, to reduce tear evaporation. Stop smoking and avoid smoke. Drink 8-10 glasses of water each day. Remind patients of the 20/20/20 rule. After 20 minutes of a visually demanding task such as reading or computer work, rest the eyes for 20 seconds by gazing at a point 20 feet away.

4: **Artificial tears:** eye drops during the day and ointment at night.

LEVEL 2: If severity of Dry eye is at this level at presentation, or patient's condition worsens: ***Tear Film BUT & Schirmer =/< 10, Then Add:***

1: Anti-inflammatory therapy: Unless ocular surface inflammation is controlled, artificial tears would not wet the ocular surface. Options available are Topical Cyclosporin A, Tacrolimus skin/eye ointment, Omega 3 fatty acids, Tetracyclines, topical Steroids. The anti-inflammatory therapy has to be continued till Schirmers test shows adequate tear production and Tear Film BUT normalises.

Tetracyclines: available as eye ointment is antibacterial, anti-inflammatory, antiangiogenic, reduce lipase production (which emulsifies the fatty acids in meibomian secretion) and stabilises the tear film.

Cyclosporin A 0.5% eye drops : increases aqueous & meibomian secretion, increases goblet cell count, decreases cytokines & inflammatory cells in conjunctiva and lacrimal glands. Hence this is the only drug that improves secretion of all three components of tear film. It has to be preservative free as preservatives kill the active ingredient. It can be easily prepared: a capsule (Syndamum Neural) contains water-miscible gel. It can be syringed out, put in a sterilized bottle and mixed with distilled water. (gel from one 25 mg capsule mixed in 5 cc makes 0.5% solution). This can be used only for a week and

made fresh weekly. It can be made in Caster oil to provide for the deficiency of lipid layer.

Tacrolimus: this has the same mechanism of action as Cyclosporin A eye drops but is 10 - 100x more potent. It is available as a skin cream 0.03% (Ecczemus, Brooke Pharma) but is safe to use in lower conjunctival fornix, causes less stinging than Cyclosporin eye drops hence patients are more compliant to therapy. The 0.1% cream can be applied to lower lid skin twice a day.

Topical Steroids: Mild steroids can be used but long-term use causes a lot of side-effects so should be avoided as better/safer options are available as mentioned above

2: **Punctal plugs**: they should be avoided till ocular surface inflammation has been controlled by the above mentioned therapy. If they are used at the start of therapy then the retained inflammatory toxins will further enhance ocular surface inflammation and will worsen the condition**.**

3: Transdermal testosterone cream: applied to the upper eyelids improved tear production and meibomian gland secretion in subjects after three weeks. Post-menopausal women showed the greatest improvement while men showed the least improvement. Since then, testosterone drops have come into use. These off-label uses of testosterone cream and drops are not yet FDA approved.

LEVEL 3: *If symptoms are severe, conj. & central corneal staining; TBUT & Schirmer's < 5mm:*

1: Permanent punctal occlusion

2: Autologous serum: Contains trophic factors which promotes growth & migration of corneal epithelial cells, immunoglobulins, vitamins & are non-antigenic, as well as preservative-free. They are contraindicated if the patient has HIV, Hepatitis B/C, anemia. Complications that can occur are bacterial keratitis, conjunctivitis, scleral vasculitis & melting but they are rarely seen if proper precautions are taken in preparation.
Preparation: Draw 60 cc blood. Allow it to clot prior for 5-6 hrs. The serum is taken which now only contains platelets but no cells; it is centrifuged at 1500 – 5000 rpm (300 – 4000 g) for 5 – 20 minutes so that platelets settle down. The serum is prepared in a clean room with a Laminar air flow hood and positive pressure (Operation theatre). To prepare 50% serum, 2.5 cc serum is added to 2.5cc normal saline in clean, sterile bottles (ETO). 30 bottles are prepared, they are frozen at -20* and then dispensed. They should be kept in freezer, one bottle should be used for 1-2 days and discarded.

3: Soft bandage contact lens

LEVEL 4: Severe symptoms, SPK+++, conj. Scarring/symblepharon, TBUT immediate, schirmer< 2mm :

- **Systemic immunosuppressant drugs.**
- **Surgery : amniotic membrane graft, lid surgery, tarsorrhaphy, cauterize punctae.**