



# **Novel Methods In Management Of Dry Eye**

*Essay*

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Ophthalmology*

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# ***Contents***

|                                           | <b><i>Pages</i></b> |
|-------------------------------------------|---------------------|
| <b>List of Abbreviation</b>               | <b><i>i</i></b>     |
| <b>List of Tables</b>                     | <b><i>iii</i></b>   |
| <b>List of Figures</b>                    | <b><i>iv</i></b>    |
| <b>Introduction</b>                       | <b><i>1</i></b>     |
| <b>Chapter 1 :</b>                        | <b><i>5</i></b>     |
| <b>Anatomy and physiology</b>             |                     |
| <b>Chapter 2 :</b>                        | <b><i>11</i></b>    |
| <b>Pathogenesis and causes of dry eye</b> |                     |
| <b>Chapter 3 :</b>                        | <b><i>17</i></b>    |
| <b>Diagnosis of dry eye disease</b>       |                     |
| <b>Chapter 4 :</b>                        | <b><i>68</i></b>    |
| <b>Treatment of dry eye disease</b>       |                     |
| <b>Summary</b>                            |                     |
| <b>References</b>                         | <b><i>134</i></b>   |
| <b>Arabic Summary</b>                     | <b><i>-</i></b>     |

## *List of Abbreviations*

|                |                                                   |
|----------------|---------------------------------------------------|
| <b>AM</b>      | <b>Amniotic membrane</b>                          |
| <b>AMT</b>     | <b>Amniotic membrane transplantation</b>          |
| <b>BAK</b>     | <b>Benzalkonium chloride</b>                      |
| <b>BSLPD</b>   | <b>Boston scleral lens prosthetic device</b>      |
| <b>CCD</b>     | <b>Charge-coupled device</b>                      |
| <b>CGVHD</b>   | <b>Chronic graft-versus-host disease</b>          |
| <b>CMC</b>     | <b>Carboxymethylcellulose</b>                     |
| <b>COX</b>     | <b>Cyclooxygenase enzyme</b>                      |
| <b>DED</b>     | <b>Dry eye disease</b>                            |
| <b>DEWS</b>    | <b>Dry eye workshop</b>                           |
| <b>DHA</b>     | <b>Docosahexaenoic acid</b>                       |
| <b>EDTA</b>    | <b>Ethylene diamine tetra acetic acid</b>         |
| <b>EEC</b>     | <b>Ectrodactyly ectodermal-dysplasia-clefting</b> |
| <b>EFAs</b>    | <b>Essential fatty acids</b>                      |
| <b>EGF</b>     | <b>Epidermal growth factor</b>                    |
| <b>EPA</b>     | <b>Eicosapentaenoic acid</b>                      |
| <b>ELISA</b>   | <b>Enzyme linked immunosorbent assay</b>          |
| <b>EPA</b>     | <b>Eicosapentaenoic acid</b>                      |
| <b>FCT</b>     | <b>Fluorescein clearance tear test</b>            |
| <b>FDA</b>     | <b>Food and drug administration</b>               |
| <b>FK</b>      | <b>Filamentary keratitis</b>                      |
| <b>GLA</b>     | <b>Gamma linolenic acid</b>                       |
| <b>HCTZ</b>    | <b>Hydrochlorothiazide</b>                        |
| <b>HIV</b>     | <b>Human immunodeficiency virus</b>               |
| <b>HPMC</b>    | <b>Hydroxypropylmethyl cellulose</b>              |
| <b>HP-guar</b> | <b>Hydroxypropyl-guar</b>                         |
| <b>HRT</b>     | <b>Hormone replacement therapy</b>                |
| <b>IAI</b>     | <b>Irregularity asymmetry index</b>               |
| <b>IBI</b>     | <b>Inter blink interval</b>                       |
| <b>IL-1</b>    | <b>Interleukin-1</b>                              |
| <b>IOP</b>     | <b>Intraocular pressure</b>                       |
| <b>KCS</b>     | <b>Keratoconjunctivitis sicca</b>                 |
| <b>LASIK</b>   | <b>Laser in situ keratomileusis</b>               |

|                  |                                               |
|------------------|-----------------------------------------------|
| <b>LFU</b>       | <b>L</b> acrimal functional unit              |
| <b>LIPCOF</b>    | <b>L</b> id parallel conjunctival folds       |
| <b>LSCD</b>      | <b>L</b> imbal stem cell deficiency           |
| <b>MGD</b>       | <b>M</b> eibomian gland dysfunction           |
| <b>NITBUT</b>    | <b>N</b> on invasive break-up time            |
| <b>NSAIDs</b>    | <b>N</b> on-steroidal anti inflammatory drugs |
| <b>OCP</b>       | <b>O</b> cular cicatricial pemphigoid         |
| <b>OPI</b>       | <b>O</b> cular protection index               |
| <b>OTC</b>       | <b>O</b> ver the counter                      |
| <b>PAS</b>       | <b>P</b> eriodic acid Schiff                  |
| <b>PVA</b>       | <b>P</b> olyvinyl alcohol                     |
| <b>RPM</b>       | <b>R</b> evolution per minute                 |
| <b>SAI</b>       | <b>S</b> urface asymmetry index               |
| <b>SH</b>        | <b>S</b> odium hyaluronate                    |
| <b>SMG</b>       | <b>S</b> ubmandibular gland                   |
| <b>SRI</b>       | <b>S</b> urface regularity index              |
| <b>SS</b>        | <b>S</b> jogren's syndrome                    |
| <b>TBUT</b>      | <b>T</b> ear break up time                    |
| <b>TCR</b>       | <b>T</b> ear clearance rate                   |
| <b>TFI</b>       | <b>T</b> ear function index                   |
| <b>TGF</b>       | <b>T</b> ransforming growth factor            |
| <b>TNF-alpha</b> | <b>T</b> umor necrosis factor-alpha           |
| <b>VEGF</b>      | <b>V</b> ascular endothelial growth factor    |
| <b>WHS</b>       | <b>W</b> omen's Health Study                  |

## ***List of tables***

| <b><i>Table No.</i></b> | <b><i>Title</i></b>                                           | <b><i>Page</i></b> |
|-------------------------|---------------------------------------------------------------|--------------------|
| 1                       | The McMonnies questionnaire .....                             | 19                 |
| 2                       | Grading of lid parallel conjunctival folds (LIPCOF)           | 27                 |
| 3                       | Grading of corneal and conjunctival staining.....             | 38                 |
| 4                       | Grading of interference of lipid layer by interferometer..... | 60                 |
| 5                       | Dry Eye Disease Severity Grading Scheme.....                  | 69                 |

## *List of Figure*

| <b>Fig. No.</b> | <b>Title</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | <b>Page</b> |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------|
| 1               | Preocular tear film layers                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 5           |
| 2               | Normal upper bulbar conjunctiva goblet cells (arrows) among the nongoblet epithelial cells. PAS stained. ....                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 8           |
| 3               | The complexity of tear film distribution and stability .....                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 9           |
| 4               | Lacrimal Functional Unit.....                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 10          |
| 5               | Mechanism of dry eye syndrome .....                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 12          |
| 6               | Classification of Dry Eye Disease .....                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 15          |
| 7               | Normal tear meniscus.....                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 25          |
| 8               | Keratoconjunctivitis Sicca, reduced tear meniscus.....                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 25          |
| 9               | Meibomian gland dysfunction.....                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 26          |
| 10              | Lid-parallel conjunctival folds highlighted by fluorescein                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 27          |
| 11              | Punctuate epithelial keratopathy.....                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 28          |
| 12              | Filaments and mucus plaques .....                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 29          |
| 13              | Schirmer test .....                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 33          |
| 14              | Thread test.....                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 35          |
| 15              | Rose Bengal staining of the conjunctiva <b>(a)</b> and cornea <b>(b)</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 39          |
| 16              | (a) PAS staining of normal impression cytology with goblet cells (asterisks) and a 1:2 nucleus-cytoplasm ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 40          |
| 16              | (b) PAS staining of metaplastic human conjunctiva with 1:12 nucleus-cytoplasm ratio (left) and snake-like condensed nuclei (right, arrows) .....                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 41          |
| 17              | In vivo laser scanning confocal microscopy                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 42          |
| 18              | In vivo confocal microscopy in a normal eye                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 43          |
| 19              | Impression cytology imprints and in vivo confocal microscopy scans from representative Sjogren syndrome(SS) patients and control subjects: (a): Conjunctival impression cytology imprint showing sheets of epithelial cells with scanty cytoplasm and large nuclei in a 42 year old female control subject. (b): Imprint from a 38 year old female SS patient shows consistently large epithelial cells with abundant cytoplasm and pyknotic nuclei. (c): Confocal microscopy scan showing sheets of densely packed small epithelial cells with large nuclei and scanty cytoplasm in the same control subject. (d): Confocal microscopy scan showing enlargement of individual superficial epithelial cells with pyknotic nuclei. Red arrow shows an area of cellular drop out..... | 44          |

| <b>Fig. No.</b> | <b>Title</b>                                                                                                                                                          | <b>Page</b> |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------|
| 20              | Tear film break-up. The beginning of tear fil break-up is visible in the lower right corner by wisps of black.....                                                    | 48          |
| 21              | Oculus keratograph.....                                                                                                                                               | 50          |
| 22              | Xeroscope images. (A) Normal patient showing uniform grid. (B) Patient with lacrimal keratoconjunctivitis, showing distortions of the grid indicated by arrows.....   | 52          |
| 23              | steps of tear function index test.....                                                                                                                                | 55          |
| 24              | Gland expression.....                                                                                                                                                 | 56          |
| 25              | loop of plastic tape.....                                                                                                                                             | 57          |
| 26              | Infrared Meibography of Normal Meibomian Glands                                                                                                                       | 58          |
| 27              | extensive meibomian gland dropout in a patient with meibomian gland dysfunction .....                                                                                 | 59          |
| 28              | Interferometry images of (a) normal eye, (b) eye with abnormal lipid layer.....                                                                                       | 60          |
| 29              | Meniscometry: demonstration of the reduced size of the tear meniscus in aqueous- deficient dry eye (L) compared to a normal tear meniscus (R) using meniscometry..... | 62          |
| 30              | Ferning test. a is class I, b is class II, c is class III, d is class IV, e is class V.....                                                                           | 66          |
| 31              | chemical composition of (a) a healthy human tear,(b) tears in chronic DED, and (c) an artificial tear                                                                 | 83          |
| 32              | Mechanism of action of anti-inflammatory drugs by blocking the Inflammation Pathway.....                                                                              | 86          |
| 33              | Insertion of a silicone punctal plug in a patient with DED .....                                                                                                      | 99          |
| 34              | The Oasis Form Fit plug.....                                                                                                                                          | 100         |
| 35              | The Smart Plug, dry (top) and warmed (bottom.....                                                                                                                     | 101         |
| 36              | <b>(a):</b> Freeman-style silicone plug on its inserter <b>(b):</b> Enlarged view of the plug.....                                                                    | 102         |
| 37              | Three sizes of Herrick lacrimal Plugs on their inserters.....                                                                                                         | 102         |
| 38              | moisture chamber spectacles.....                                                                                                                                      | 107         |

| <b><i>Fig. No.</i></b> | <b><i>Title</i></b>                                                                                                                                                                                                                                                                                                                                                                                             | <b><i>Page</i></b> |
|------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|
| 39                     | Boston scleral lens prosthetic device                                                                                                                                                                                                                                                                                                                                                                           | 112                |
| 40                     | Punctal patching with autologous conjunctiva. (A) Ectropionization of the lacrimal punctum, a square incision around the punctum. (B) Excision of the superficial epithelial and subepithelial tissue inside the square. (C) Excision of a square of bulbar conjunctiva of the same eye. (D) Suture of the transplanted patch onto the lacrimal punctum.....                                                    | 118                |
| 41                     | Punctal blepharorrhaphy. (A) A 3 X 2.5 mm parallelopiped margin of superficial tissue is excised from the medial part of both lids, including the lacrimal puncta, leaving a raw surface. (B) The four corners of one of the raw rectangles are sutured to the corresponding corners of the contra-altitudinal lid. Thus, the effect of the punctal occlusions is added to that of the medial tarsorrhaphy..... | 121                |





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## ***INTRODUCTION***

Dry eye syndrome (DES) is a multifactorial disease of the tears and the ocular surface that results in discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface. DES is also called more recently, dysfunctional tear syndrome (***Perry, 2008***). Multiple causes can produce either inadequate tear production or abnormal tear film constitution, resulting in excessively fast evaporation or premature destruction of the tear film. (***Stephen, 2012***)

The human tear film plays a vital role in the maintenance of optical clarity as well as in ocular surface protection, lubrication, and nourishment. It is made up of three layers. The outer most the lipid layer secreted by meibomian glands, dysfunction of which results in evaporative dry eye. Middle aqueous layer secreted by the lacrimal gland, deficiency of this layer results in hyposcretive dry eye. The inner most is the mucin layer secreted by the conjunctival goblet cell, crypts of Henle and glands of Manz. Deficiency of this layer is the feature of both hyposcretive and evaporative state. (***Rahman et al., 2007***)

DES can be classified into two main categories, tear deficient dry eye and evaporative dry eye. The tear deficient dry eye is subdivided into two categories: Sjogren syndrome tear deficiency and non-Sjogren tear deficiency depending upon whether there are associated systemic signs and symptoms or not. ***(Peters and Colby ,2007)***

Dry eye disease (DED) patients may experience foreign body sensation, burning, itching or redness of the eyes, blurred vision and photophobia. ***.(Belmonte et al , 2004)***

These symptoms are often exacerbated in smoky or dry environments, by indoor heating, or by excessive reading or computer use. ***(Stephen, 2012)***

These symptoms are quantified objectively in The McMonnies questionnaire, which includes 14 questions given to the patient to fill out, which is used to screen patients for the possibility of dry eye disease. ***(McMonnies and Ho, 2004)***

In DES, symptoms tend to be worse toward the end of the day, with prolonged use of the eyes, or with exposure to extreme environmental conditions. Patients with meibomian gland dysfunction (MGD) may complain of redness of the eyelids and conjunctiva, but in these patients, the symptoms are worse on awakening in the morning. Paradoxically, some patients with DES

complain of too much tearing. When evidence of DES exists, this symptom often is explained by excessive reflex tearing due to severe corneal surface disease from the dryness. Certain systemic medications also decrease tear production, such as antihistamines, beta-blockers, and oral contraceptives.**(Perry, 2008)**

DED is essentially a clinical diagnosis, made by combining information obtained from the history and from the physical examination and performing one or more tests to lend some objectivity to the diagnosis. No single test is sufficiently specific to permit an absolute diagnosis of DES.**(Stephen, 2012)**

For patients with moderate to severe dry eye diagnosis can be made by one or more of the standard clinical tests, namely fluorescein, rose bengal or lissamine green staining, tear-film breakup time, Schirmer's tests and fluorophotometry, impression cytology and tear osmolarity test.**(Abelson, 2011 )**

In vivo laser scanning confocal microscopy seems to be an efficient non-invasive tool in the evaluation of phenotypic alterations of the conjunctival epithelium in dry eye disease.**(kojima et al, 2010)**

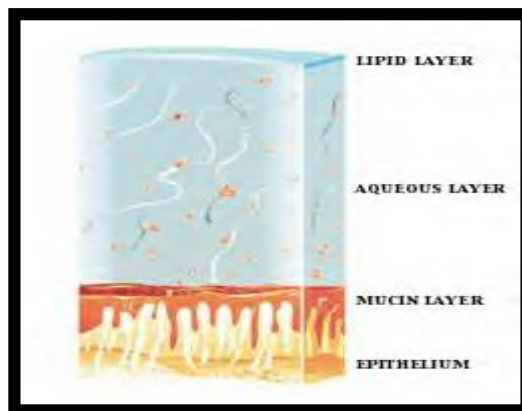
Also oculus keratograph has a scanning softwar that can non-invasively assess the tear film ,providing both quantitative and qualitative assessments by using corneal topography.( **koury, 2011**)

The International Dry Eye WorkShop (DEWS) Subcommittee members reviewed an approach for the management of DED which is based on disease severity ranging from education and environmental/dietary modifications, preserved and preservative-free artificial tear substitutes, anti-inflammatory agents, topical corticosteroids, topical cyclosporine A, topical/systemic omega-3 fatty acids, tetracyclines, punctal plugs, secretagogues, moisture chamber spectacles, Autologous serum up to surgical options, which include cisternoplasty, tarsorrhaphy (partial or complete), Mucous membrane grafting, salivary gland duct transposition, conjunctival graft of the minor salivary gland and aminiotic membrane transplantation. (**Stephen,2012**) In addition to limbal or stem cell transplantation. (**Hyon et al., 2007**)

## ***Anatomy And Physiology Of Preocular Tear Film***

Tear film is a thin film of fluid which covers the exposed ocular surface and essential for the health and normal function of the eye and visual system.**(Dartt et al, 2011)** Its overall purpose is to maintain the corneal clarity and the quality of the image projected onto the retina. The corneal clarity depends, in turn , on the integrity of the tear film and the health of the ocular surface.  
**(Pleyer and Mondino, 2004)**

***The normal preocular tear film*** is formed of three layers from anterior to posterior (**fig.1**): a thin superficial lipid layer, a thicker aqueous layer and a very thin mucoid layer covering the corneal epithelium. **(Kanski et al., 2011)**



**Fig.(1)** Preocular tear film layers **(Kanski et al., 2011)**

### **(1) Outer lipid layer :**

The lipid layer is approximately 0.1  $\mu\text{m}$  thick. This superficial layer is secreted by Zeis and Meibomian glands of the lid. The thickness of the layer can be increased by forced blinking and conversely reduced by infrequent blinking. *(Xuan et al., 2001)*

It is composed of a polar phase containing phospholipids lie adjacent to the aqueous-mucin interface and a non-polar phase containing waxes, cholesterol, esters and triglycerides lie at the tear-air interface. The polar lipids are bound to lipocalins within the aqueous layer, which are small secreted proteins that have an important role in stabilizing the tear-film lipid layer by transferring lipids to it from the aqueous layer. *(Mochizuki et al., 2009)*.

The function of this layer is to prevent evaporation of the aqueous layer to maintain tear film thickness and to act as a surfactant allowing spread of the tear film. *(kanski et al., 2011)*

### **(2) Middle aqueous layer :**

This layer is about 8  $\mu\text{m}$  thick, comprising most of the tear film thickness. The main lacrimal glands produce about 95% of the aqueous component of tears and the accessory lacrimal glands of Krause and wolfring produce the reminder. It is composed of water, electrolytes, dissolved mucin, proteins, growth factors driven from