Correlation of Bacterial Burden, Meibomian Gland Dysfunction and Ocular Surface Disease

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Meibomian Gland Dysfunction and Ocular Surface Disease

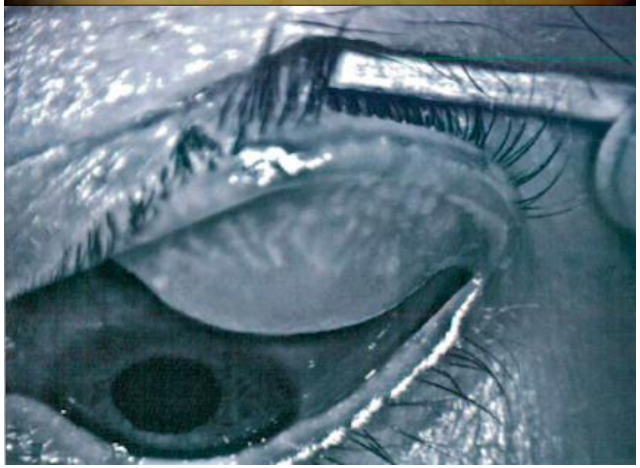
NORMAL

Meibomian glands: modified sebaceous glands arranged vertically in the tarsal plate[1,16]

With each blink, meibum is released & interacts with the tear film to create a smooth refractive surface[1,16]

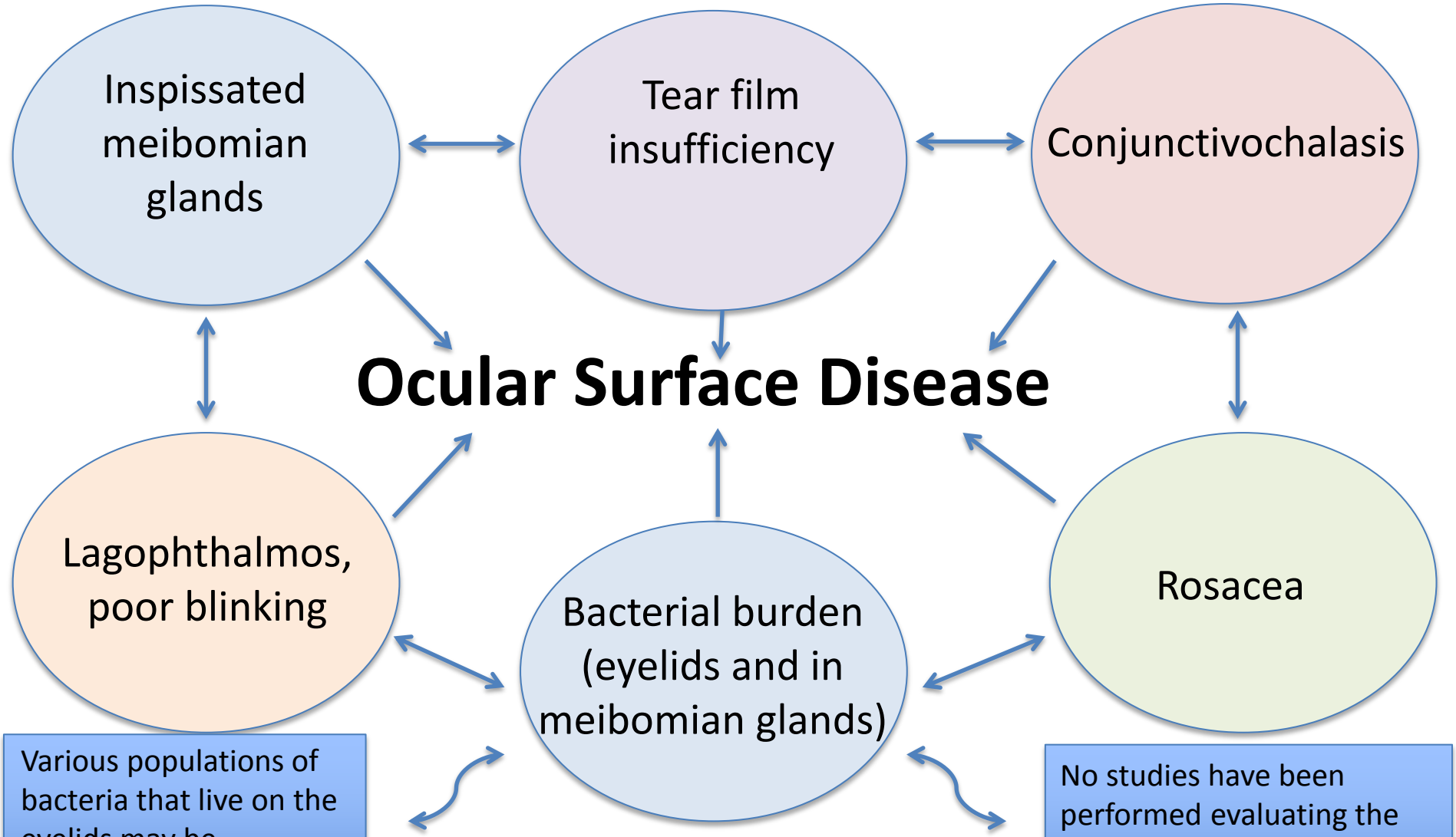
Patients with meibomian gland dysfunction (MGD) → visual changes, tear film instability, reduced tear break up time and evaporative dry eye [1,16]

ABNORMAL



Left untreated, MGD will cause or exacerbate dry eye symptoms (dryness, burning, itching, foreign body sensation, photophobia, tearing, intermittent blurred vision)[1,12-16]

What is the ultimate underlying etiology?

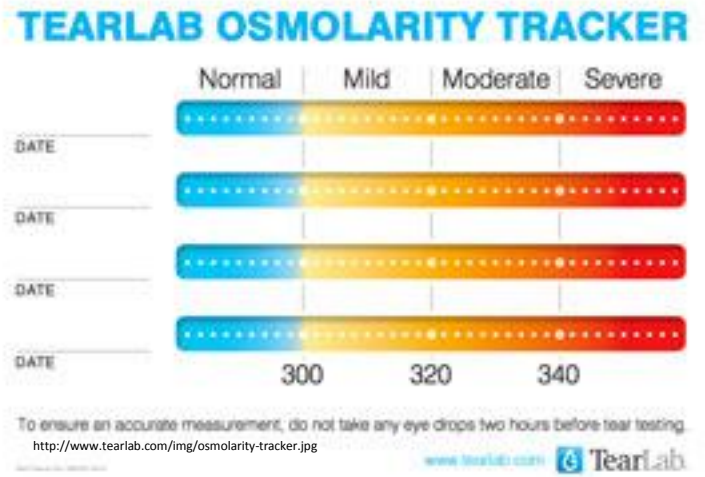


Various populations of bacteria that live on the eyelids may be implicated in either the etiology or propagation of MGD

What should we treat?

No studies have been performed evaluating the correlation of bacterial load on specific dry eye/ocular surface disease markers [3,5,8-10]

The Ocular Surface Diagnostic Armamentarium

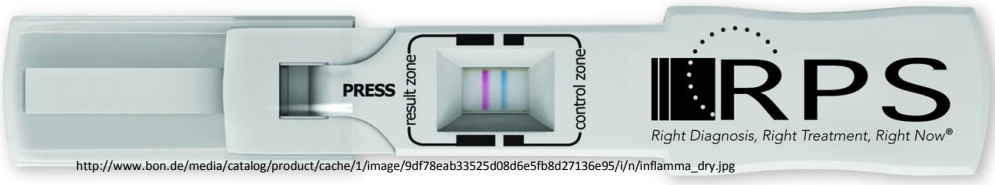


http://www.tearlab.com/img/osmolarity-tracker.jpg

- Tear osmolarity testing (TOT): degree of electrolyte concentration in the tears
  - ⇧TOT = low level of aqueous component of the tears[6].

http://www.optometricmanagement.com/archive/2008/December/Supplements/OM_367/images/OM_AlconNGS_Suppl_December_A01_Fig03.jpg

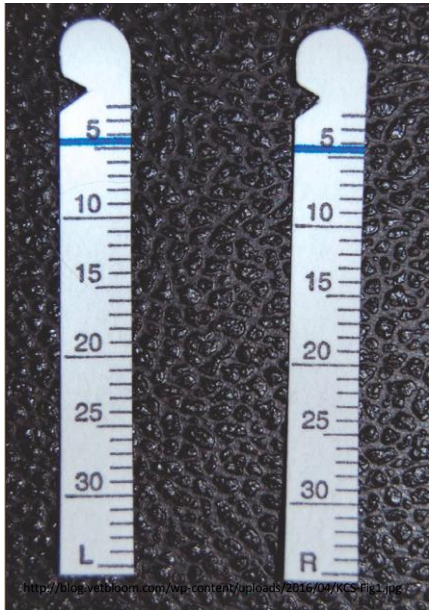
- Lissamine green (LG): degree of ocular surface disruption/disease (1,2,6)



http://www.bon.de/media/catalog/product/cache/1/image/9df78eab33525d08d6e5fb8d27136e95/i/n/inflamma_dry.jpg

- Inflammatory marker matrix metalloproteinase-9 (MMP-9) presence in the tears
  - Positivity suggests favorable response to anti-inflammatory therapy[6,15].

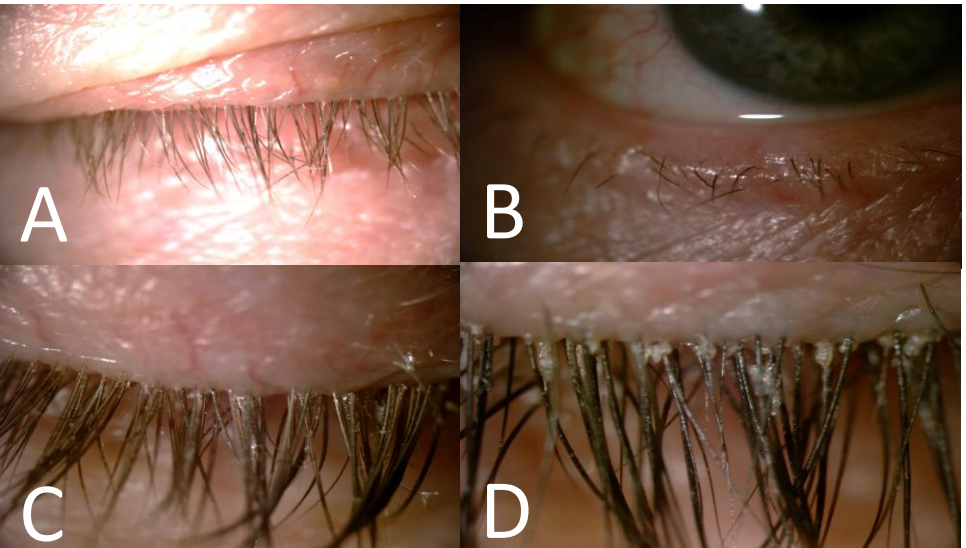
- Schirmer I test: evaluates for aqueous deficiency



http://blog.vetbloom.com/wp-content/uploads/2016/03/KCS-Fig1.jpg

Objectives

- Evaluate bacterial flora on the eyelid margin and within meibomian gland secretions across MGD spectrum
- Evaluate the correlation of bacterial burden on specific dry eye parameters:
  - TOT
  - Meibography
  - Schirmer 1 testing
  - Tear MMP-9 levels
  - Lissamine green staining of the ocular surface



Study Population

4 groups, 10 patients each (20 eyes per group)

- Prospective, observational, single center study
- Both eyes evaluated for each patient

Group A: Control group

- Patients without prior dx or frank evidence of dry eye/MGD on exam

Group B: Asymptomatic patients with some evidence of meibomian gland dysfunction

- Patients scheduled for routine eye exams without complaint of eye irritation/dryness/redness with mild signs of MGD/dry eye

Group C: Subclinical disease

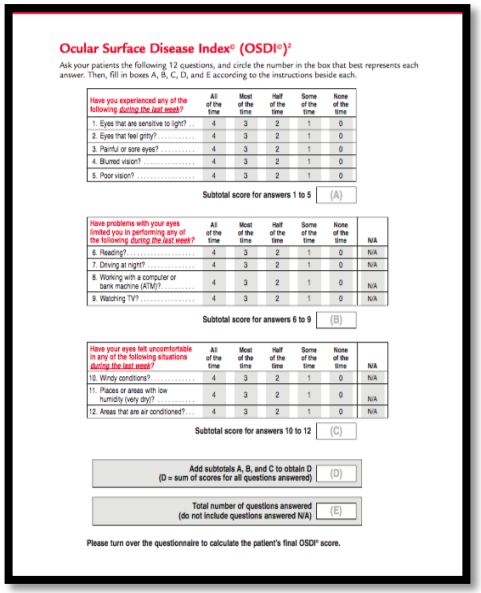
- Patients with occasional complaints of dryness, irritation, redness (symptoms related to MGD/dry eye)
- Evidence of mild-moderate MGD on exam

Group D: Clinically significant MGD

- Patients with complaints of near constant burning/irritation/dryness/redness
- Significant disease (meibomian gland plugging/drop out, LG staining of the ocular surface, positive dry eye markers) on exam

Evaluation

- Medical/surgical/ocular history
- Ocular Surface Disease Index (OSDI) Questionnaire
- Visual Acuity assessment
- Comprehensive slit lamp examination
- Lissamine green staining: cornea & conjunctiva
- Meibomian gland expression: ease of expression and type of secretion noted (e.g. liquid, oily, thick, purulent, inspissated)
- TOT/MMP-9/Schirmer I
- Meibography: Grading of appearance, % gland drop-out
- Cultures of lid margins and meibum: blood, chocolate and Sabouraud agar
- Gram stain of lid margins and meibum
- Cytology of lid margins and meibum



Ocular Surface Disease Index® (OSDI®)²

Ask your patients the following 12 questions, and circle the number in the box that best represents each answer. Then, fill in boxes A, B, C, D, and E according to the instructions beside each.

Have you experienced any of the following *during the last week*?	All of the time	Most of the time	Half of the time	Some of the time	None of the time
1. Eyes that are sensitive to light?	4	3	2	1	0
2. Eyes that feel gritty?	4	3	2	1	0
3. Painful or sore eyes?	4	3	2	1	0
4. Blurred vision?	4	3	2	1	0
5. Poor vision?	4	3	2	1	0

Subtotal score for answers 1 to 5 (A)

Have problems with your eyes limited you in performing any of the following *during the last week*?	All of the time	Most of the time	Half of the time	Some of the time	None of the time	N/A
6. Reading?	4	3	2	1	0	N/A
7. Driving at night?	4	3	2	1	0	N/A
8. Working with a computer or bank machine (ATM)?	4	3	2	1	0	N/A
9. Watching TV?	4	3	2	1	0	N/A

Subtotal score for answers 6 to 9 (B)

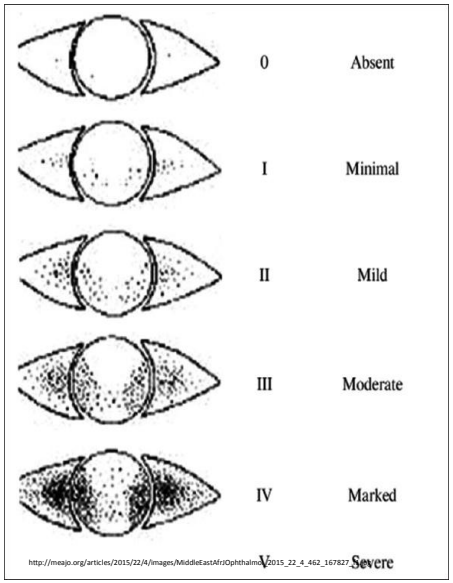
Have your eyes felt uncomfortable in any of the following situations *during the last week*?	All of the time	Most of the time	Half of the time	Some of the time	None of the time	N/A
10. Windy conditions?	4	3	2	1	0	N/A
11. Places or areas with low humidity (very dry)?	4	3	2	1	0	N/A
12. Areas that are air conditioned?	4	3	2	1	0	N/A

Subtotal score for answers 10 to 12 (C)

Add subtotals A, B, and C to obtain D (D = sum of scores for all questions answered) (D)

Total number of questions answered (do not include questions answered N/A) (E)

Please turn over the questionnaire to calculate the patient's final OSDI® score.



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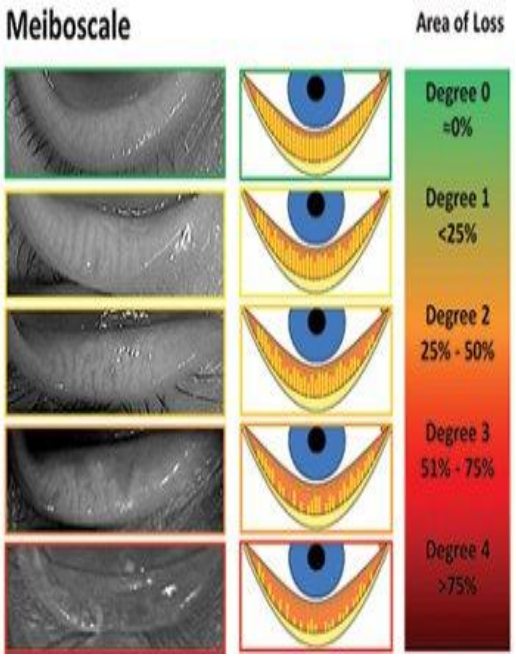
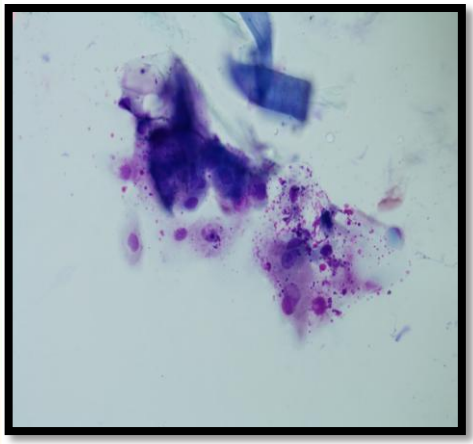
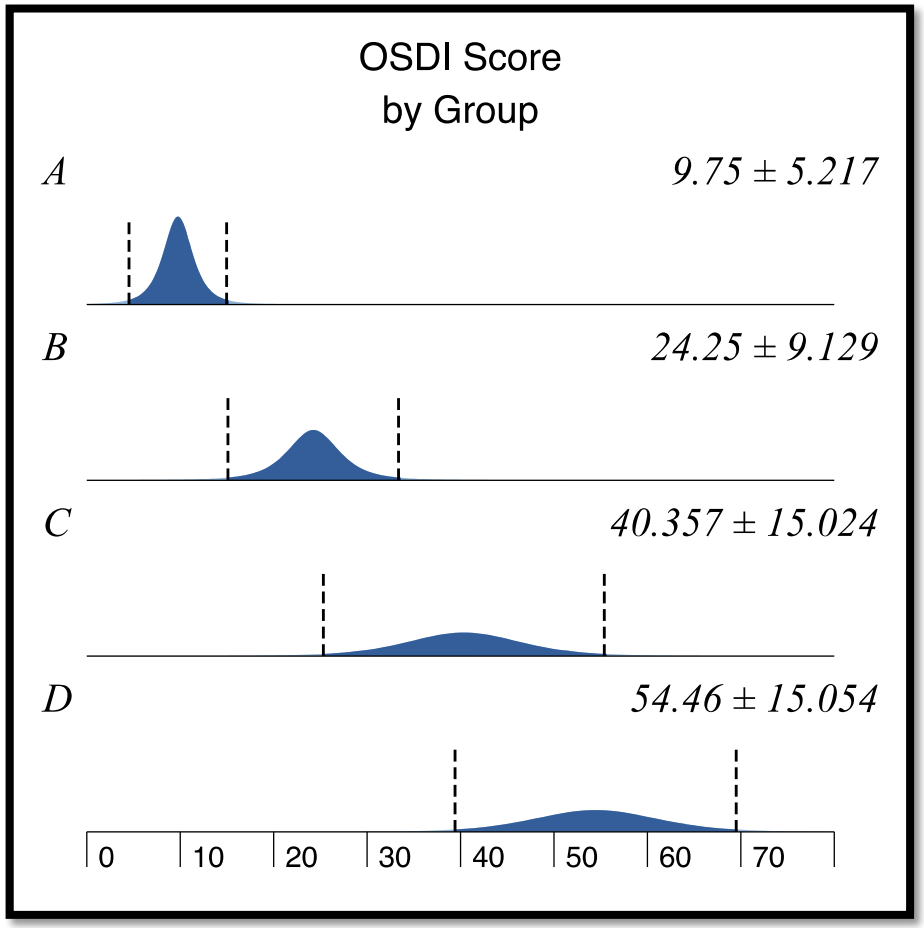




Results – Demographics, Stratification

- Group A patients were younger on average (44 years)
  - Group B = 69 years
  - Group C= 60.43 years
  - Group D= 56.7 years
- Females predominated in Group B (75%), C (76%), and D (89%), compared with Group A (50%).
  - No statistically significant difference for age or sex between groups in terms of ocular surface testing and culture results
- Average OSDI score was higher in Group D (54.5) compared to all other groups
    - Graph 1
  - Group A: 9.75
  - Group B: 24.25
  - Group C: 40.36
  - This was statistically significant (ANOVA, $p<0.001$).



Graph 1: OSDI Score by group

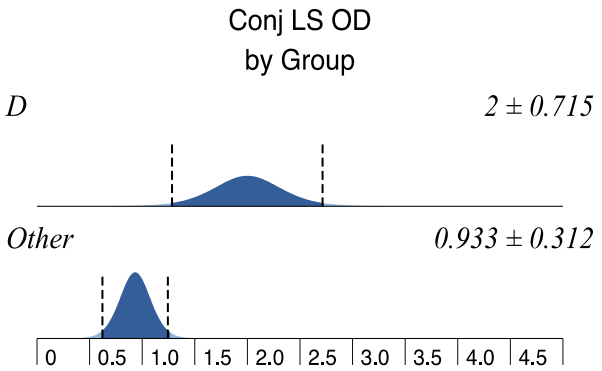
Results - Testing

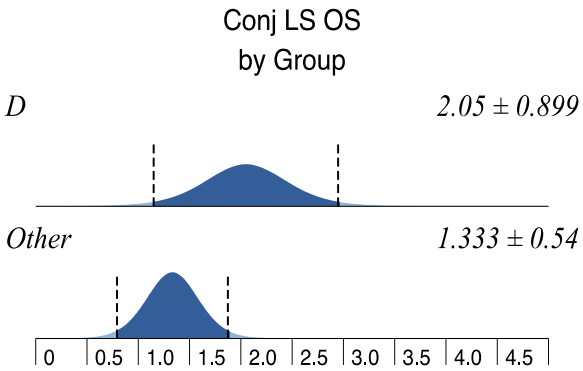
GROUP	TOT	Schirmer I	MMP-9 (% Positive)
A	312.5	15.13	25%
B	300.75	7.63	50%
C	304.57	16.43	57%
D	301.7	12.7	55%

There were no statistically significant differences in TOT, Schirmer I scores or MMP-9 testing between groups

Results - Lissamine Staining

Graph 2:
t-test, p= 0.002

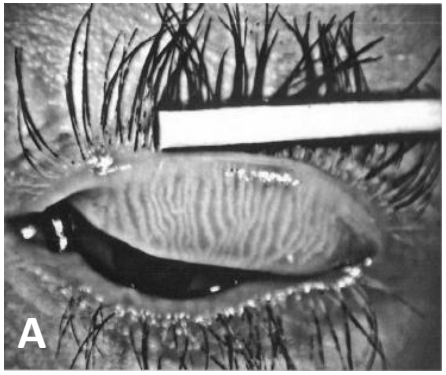


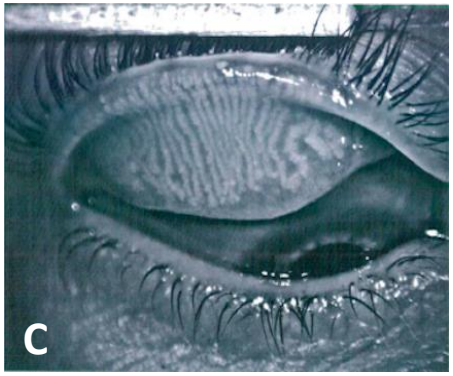


Graph 3:
t-test, p=0.122

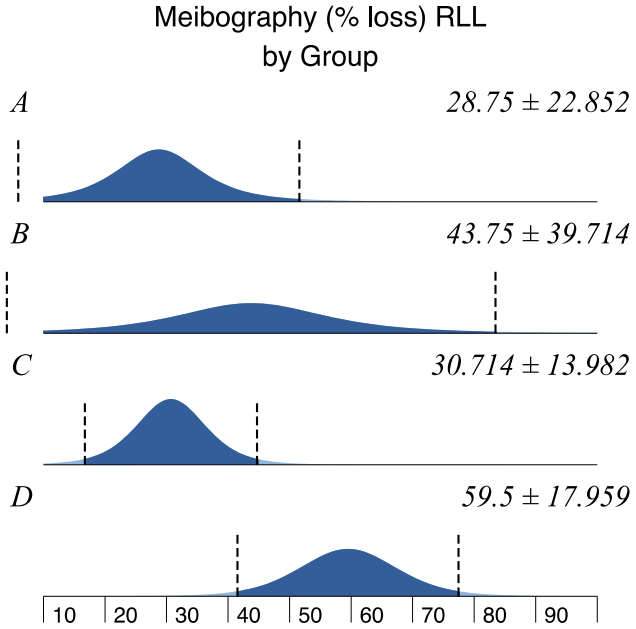
- Average grade of **conjunctival** LG staining was worse in Group D
  - When comparing degree of LG conjunctival staining of Group D to the other groups, the level of staining of the right eye was statistically significant (*Graph 2*)
  - Although the staining of the conjunctiva was higher for the left eye in Group D compared to other groups, this was not statistically significant (*Graph 3*)
- Grade of **corneal** LG staining was similar across all groups and was not statistically significant

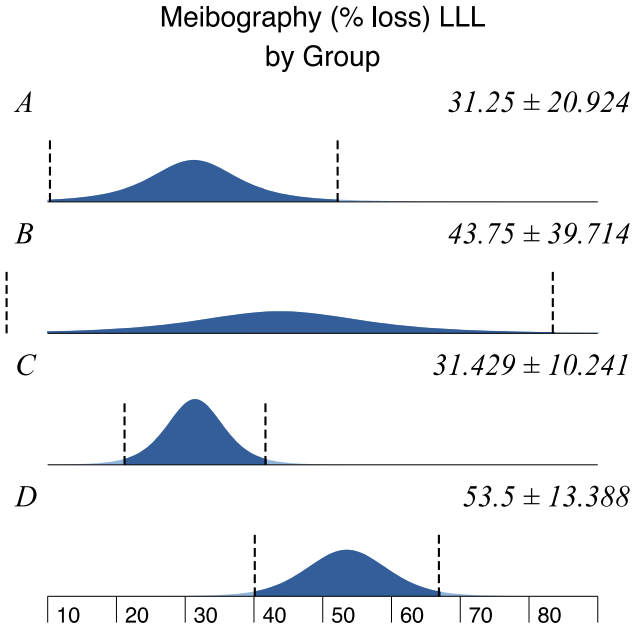
Results - Meibography





Graph 4: ANOVA, p=0.006





Graph 5: ANOVA, p=0.013

- Meibography demonstrated greater % drop-out/loss of gland scores in Group D
  - This was statistically significant for the RLL (Graph 4) and LLL (Graph 5)
  - Although a difference was seen in the RUL and LUL in Group D compared to all other groups, this was not statistically significant.

Results - Cultures

GROUP	+ Lid Cx	+ MG Cx	+ Gram Stain (lid)	+ Gram Stain (MG)	+ Cytology (lid)	+ Cytology (MG)	Coag Neg Staph +	Other Organism +
A	0	0	0	0	0	0	0	0
B	0	0	0	0	0	0	0	0
C	21.5%	0	0	0	0	0	100%	66%
D	25%	20%	0	0	0	0	60%	60%

- Culture positivity across groups was not statistically significant, including organism type
- Additional organisms present on culture for *Group C* included Bacillus spp (*not anthracis*) and Corynebacterium spp
- Additional organisms present on culture for *Group D* included Actinomyces spp, Corynebacterium spp, Strenophonomonas maltophilia, Pantoea agglomerans, and Bacillus spp (*not anthracis*)
- 40% of all cultures were resistant to erythromycin
- 100% of all cultures were sensitive to tetracycline
  - These results were not statistically significant
- For the *Group D* patients with both positive lid margin and meibomian gland cultures, the cultures demonstrated the same organisms.
  - This was not statistically significant

Discussion

- Our findings are in agreement with previous publications demonstrating predominance of coagulase negative Staph species on the eyelid margins and within meibomian gland secretions
- There was no significant correlation between bacterial burden or species with degree of meibomian gland dysfunction, dry eye diagnostic markers
- There was significant correlation with severe meibomian gland dysfunction and conjunctival lissamine green staining indicating a relationship between ocular surface disease and meibomian gland dysfunction
- Although bacterial burden is implicated in the etiology and propagation of meibomian gland disease and several treatments are available to modify this (i.e. antibiotics, lid hygiene, Blephex^{R}), our study showed a lack of clear correlation between bacterial burden and severity of disease as well as with various dry eye/ocular surface disease markers
- Perhaps treatments aimed at reducing bacterial burden should be reconsidered, and treatments directed more towards decreasing MGD and increasing tears and tear-film regularity on the ocular surface should be emphasized

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