8:00 AM 2 hours | Room 225 A-B
P-04 | **Papers: Ocular Surface**
Moderators: Gary Foulks, MD, FACS, Sruthi Srinivasan, PhD, BSOptom, FAAO

8:00 AM. **TNF-ALPHA MRNA EXPRESSION IN AQUEOUS DEFICIENT DRY EYE** (120007)

Barbara Caffery, OD, PhD, FAAO, Toronto, Ontario, Canada, Elizabeth M. Joyce, BSc, RT, Miriam Heynen, MSc, University of Waterloo School of Optometry and Vision Science, Robert Ritter, PhD, Alcon Research Ltd, Lyndon W. Jones, PhD, FCOptom, FAAO, University of Waterloo, Centre for Contact Lens Research

RESULTS: TNF-alpha gene expression was found to be significantly higher in the SS group (2.48+/-1.79) compared to both non-SS DE (0.95+/-1.18; $p<0.05$) and NDE (0.84+/-0.51; $p<0.05$) groups. No difference in gene expression was found between the non-SS DE and NDE groups.
PURPOSE: To quantify conjunctival epithelial TNF-alpha mRNA expression in Sjogren's Syndrome (SS), non-Sjogren's syndrome aqueous deficient dry eye (non-SS DE)and non- dry eye controls (NDE).
METHODS: 76 subjects were recruited for this study: 25 SS (confirmed via American-European Consensus Criteria 2002), 25 non-SS DE (confirmed by symptoms and Schirmer scores ≤ 10mm) and 26 NDE. Superior and temporal bulbar conjunctival epithelial cells were collected via impression cytology. Epithelial RNA was extracted and TNF-alpha gene expression was quantified by real time qPCR.
CONCLUSIONS: These results demonstrate that SS aqueous deficient dry eye is associated with a significant up-regulation of TNF-alpha, which is considered one of the primary mediators of inflammation. The degree to which TNF-alpha is up-regulated may contribute to the severe ocular surface damage observed in Sjogren's syndrome.
ADDITIONAL COMMENTS: This work is part of my PhD thesis research completed at University of Waterloo and was sponsored in part by Alcon pharmaceuticals.

8:15 AM. **LIFITEGRAST: A NOVEL TREATMENT FOR DRY EYE DISEASE** (120704)

Kelly K. Nichols, OD, PhD, FAAO, University of Houston College of Optometry, Charles Semba, MD, San Francisco, CA

RESULTS: In the first trial, lifitegrast 5.0% demonstrated significant improvements ($p<0.05$) in signs and symptoms of dry eye. Lifitegrast was safe and well-tolerated. The most common ocular adverse event was stinging/irritation upon initial instillation. There were no serious ocular or non-ocular adverse events observed during the trial. Results regarding the second trial will be presented.
PURPOSE: Dry eye disease (DED) is a chronic and debilitating disease that has a significant impact on a patient's ocular health and quality of life. Inflammation due to activated T-cells is widely accepted as central to many types of DED. An important instigator of this inflammation is the binding of two cell-surface proteins: lymphocyte function-associated antigen-1 (LFA-1) and intercellular adhesion molecule-1 (ICAM-1).

These proteins are key regulators of T-cell activation, migration, and proliferation, making it a validated and ideal target for halting inflammation in dry eye. Lifitegrast is a novel small-molecule integrin antagonist specifically built to act as an ICAM-1 decoy, thus preventing the binding of LFA-1 to ICAM-1. The purpose is to present results from two large clinical trials of lifitegrast ophthalmic solution for the treatment of DED.
METHODS: Two multicenter, prospective, randomized, double-masked, placebo-controlled trials were conducted across the US. In the first trial, 230 subjects with DED received lifitegrast ophthalmic solution (0.1%, 1.0% or 5.0%) or placebo twice-daily for 12 weeks. In the second trial, 588 patients with DED received lifitegrast ophthalmic solution, 5.0%, or placebo twice-daily for 12 weeks. Endpoints assessed in both trials included inferior and total corneal fluorescein staining score, lissamine green staining score, Ocular Discomfort Score, and OSDI (Ocular Surface Disease Index) score.
CONCLUSIONS: Treatment with twice-daily lifitegrast ophthalmic solution demonstrated significant improvement in key signs and symptoms of dry eye, was safe and well-tolerated, and may provide a welcome addition to the dry eye treatment armamentarium.
ADDITIONAL COMMENTS: Funding: SARcode Bioscience

8:30 AM. **THE UPPER AND LOWER EYE LIDS MAY NOT MAKE COMPLETE CONTACT EVEN WHEN THE LIDS APPEAR CLOSED** (120382)
Donald R. Korb, OD, FAAO, Boston, MA, Caroline Blackie, OD, PhD, FAAO, TearScience

RESULTS: Asymptomatic: 10 complete blinks did not alter the drop appearance in 28 of the 30 tested lid regions. The mean number of lid squeezes to alter the drop for each lid section was: T = 1.5+/-1.3, C = 1.9+/-1.8, N = 1.2+/-0.8. The mean number of functional MGs per lid section: T = 0.8+/-2.2, C = 4.3+/-2.3, N = 4.4+/-0.8. Symptomatic: 10 complete blinks did not alter the drop appearance in 12 of 18 tested regions (for the 6 regions where the blink did alter the drop, the number of blinks ranged from 1-6 blinks). The mean number of lid squeezes to alter the drop for each lid section was: T = 1.0+/-0.6, C = 1.2+/-1.0, N = 1.0+/-1.1. The mean number of functional MGs per lid section: T = 0.2+/-0.4, C = 3.8+/-2.7, N = 4.0+/-1.4.
PURPOSE: To investigate whether the keratinized portions of the upper and lower eyelid margins make complete contact during deliberate blinking.
METHODS: 16 subjects asymptomatic (n = 10, mean age =21.7+/-1.5 yr) and mildly symptomatic (n = 6, mean age = 21.3+/-0.5 yr) for dry eye were enrolled. Using a custom application device, a 0.1 microliter drop of unpreserved 2% liquid fluorescein (B&L, Chauvin, France) was placed on the temporal (T) third of the keratinized lower lid margin, anterior to the Line of Marx (LOM), between and slightly anterior to two meibomian gland (MG) orifices. The drop was viewed under 16x magnification. If 10 complete blinks did not alter or spread the drop, the subject was instructed to squeeze their lids shut. The number of lid squeezes required until the drop appearance was altered was recorded. This was repeated for the central (C) and nasal (N) sections. Next, standardized diagnostic MG expression was performed along the lower lid margin to assess MG functionality.
CONCLUSIONS: Counterintuitively, the keratinized portions of the upper and lower lid

margins, over 90% of the width of the margins in mildly symptomatic and asymptomatic subjects, frequently do not fully contact each other during complete blinking.

8:45 AM. **USE OF RETROILLUMINATION AS A NON-INVASIVE TECHNIQUE TO QUANTIFY THE AREA AND SLOPE OF TEAR FILM BREAKUP** (120585)

Adam Winkeler, OD, Carolyn G. Begley, OD, MS, FAAO, Larry N. Thibos, PhD, FAAO, Arthur Bradley, PhD, Robert Welch, Indiana University School of Optometry

RESULTS: In the presence of TBU, integrated RI images closely agreed with relative changes in tear film thickness measured from FL intensity, showing increasing correlation as TBU developed. Similarly, the slope of the FL image (derivative) showed increasing correlation with changes in RI image intensity as TBU developed. In areas of corneal FL staining, FL intensity changed little with time after a blink while RI intensity changes indicated TBU development. Over time, FL intensity decreased reaching a minimum within areas of TBU, suggesting full thickness breaks. The estimated mean (+/- SD) thinning rate across subjects was 15.2+/-9.3 um/min assuming a 3um initial tear film thickness.

PURPOSE: To investigate the development and spatial patterns of tear film breakup (TBU) using retroillumination imaging in conjunction with fluorescein imaging.

METHODS: A slit-lamp biomicroscope was modified to emit simultaneous widefield blue and near infrared light for fluorescence (FL) and retroillumination (RI) imaging. Two cameras simultaneously collected images of local changes in TBU following instillation of fluorescein dye and 0.5% proparicaine (5 subjects). Images were registered and spatiotemporal changes in tear film thickness within select areas of TBU were compared. Tear film thinning rates within these areas were estimated using published tear film thickness values (King-Smith et al, 2004). For each frame, RI intensity was integrated across areas of TBU and correlated with FL intensity. The derivative of Fl intensity across these areas was also correlated with RI intensity (Himebaugh et al, 2003).

CONCLUSIONS: Retroillumination of the tear film provides measures of TBU that agree well with FL imaging and may be used independently to assess changes in tear film thickness over time. This technique allows for high-resolution, noninvasive tracking of TBU over areas of corneal FL staining. By directly measuring the slope of the tear film, RI imaging may provide a simple in vivo tool to assess corneal or contact lens wetability.

ADDITIONAL COMMENTS: NEI grant 1R01EY021794-01

9:00 AM. **OPTIMIZATION OF ASSESSMENT AND GRADING FOR LID WIPER EPITHELIOPATHY** (120241)

Jalaiah Varikooty, MSc, BMed, Nancy J. Keir, OD, PhD, FAAO, Lyndon W. Jones, PhD, FCOptom, FAAO, University of Waterloo, Centre for Contact Lens Research

RESULTS: LWE was optimally visualized 3-5 minutes after 2 instillations of 10µl of 2% NaFl dye, separated by an interval of 1 minute. With LG dye, 2 strips moistened with 50µl are preferred to 1 strip, and 2 instillations separated by 1 minute provided better visualization of LWE when viewed after 3 minutes. A decrease in intensity over time after instillation was noted with NaFl and with LG in all 3 phases.

PURPOSE: Contact lens wear may be associated with upper lid margin staining, typically referred to as "lid wiper epitheliopathy" (LWE). Studies have evaluated this staining with different concentrations, volumes and methods of instilling sodium fluorescein (NaFl), lissamine green (LG) and Rose Bengal (RB) dyes, but these staining procedures have not been standardized. The objective of this study was to determine optimal techniques for demonstrating LWE with NaFl and LG.
METHODS: Five non-contact lens wearers completed the contralateral eye, crossover study, which consisted of 3 phases, each evaluating LWE-associated staining with NaFl and LG. Phases 1, 2, and 3 assessed the impact of concentration, volume and effect of repeat applications of each dye, respectively. The optimal outcome of each phase was used in each subsequent phase. Images were captured at 8x magnification through a Canon digital camera attached to a slit-lamp at 0, 3 and 5 minutes after dye instillation. At each visit a contralateral comparison was made between the participant's RE and LE, to subjectively identify the eye demonstrating the clearest staining with sufficient intensity to be easily observed. Images were also measured and analyzed using ImageJ software.
CONCLUSIONS: Optimal use of NaFl and LG dyes may assist in more accurate visualization and grading of LWE that could be correlated with symptoms of discomfort and dryness to better understand upper lid margin disease and LWE.
ADDITIONAL COMMENTS: Financial support for this study was provided by Alcon.

9:15 AM. **LID MARGIN STAINING IS ASSOCIATED WITH OSMOLARITY, CORNEAL AND CONJUNCTIVAL STAINING** (120066)
Moneisha Gokhale, BSOptom, Blanka Golebiowski, PhD, Michele Madigan, PhD, Noor Badarudin, MScOptom, Fiona Stapleton, MCOptom, PhD, FAAO, University of New South Wales, School of Optometry and Vision Science

RESULTS: Participants were aged between 18-75 years (mean 35 ± 14yrs), with 65% females. There were significant correlations ($p < 0.05$) between the upper lid margin staining and osmolarity($r = 0.27$), corneal staining ($r = 0.25$) and conjunctival staining ($r=0.43$). Corneal and conjunctival staining were also associated ($r = 0.44$). The lower lid margin staining correlated with conjuntival staining ($r = 0.38$) only. The median (range) values of the measurements were: upper lid staining= 1 (0-1), lower lid staining= 1.5 (0.5- 3), corneal staining= 0.5 (0- 3.5), conjunctival staining= 1 (0-12.5) and osmolarity= 291 mOsmol/L (278- 326). These associations were similar in contact lens and non lens wearing participants.
PURPOSE: To evaluate associations between lid margin staining, tear osmolarity and corneal and conjunctival staining.
METHODS: A cross-sectional study involving 76 participants (37 contact lens wearers) was conducted. Measures included upper and lower lid margin staining (lissamine green, modified Korb scale), corneal (fluorescein) and conjunctival (lissamine green) staining (modified Oxford scale) and in situ osmolarity (TearLab). Spearman correlation coefficient was calculated to determine significant associations.
CONCLUSIONS: The upper lid margin staining is associated with an increase in osmolarity, corneal and conjunctival staining. This highlights the need for clinicians to evaluate the upper lid margin staining during routine ocular surface examination.

ADDITIONAL COMMENTS: Blackmores Ltd,TearLab Corp, Cornea & Contact Lens Society of Australia

9:30 AM. **APPLICATION OF DIAGNOSTIC ALGORITHMS FOR DRY EYE AND MGD** (120684)

Jillian F. Meadows, OD, MS, San Francisco, CA, Lisa Jones-Jordan, PhD, FAAO, The Ohio State University College of Optometry, Jason J. Nichols, OD, PhD, FAAO, Kelly K. Nichols, OD, PhD, FAAO, University of Houston College of Optometry

RESULTS: For the purposes of initially classifying subjects in roughly equivalent groups, the Schaumberg questionnaire was used to define dry eye and non-dry eye, with 212 subjects placed into the dry eye group and 227 in the non-dry eye group. Based on a strict interpretation of the MGD report algorithm, 72 subjects were diagnosed with MGD, and 367 were diagnosed as non-MGD. Those subjects diagnosed with MGD were further categorized by severity: 3 subjects were classified as stage 1, 63 subjects were classified as stage 2 (minimal to mild symptoms and clinical signs and limited to no staining), and 6 subjects were classified as stage 3 (moderate symptoms and clinical signs and mild to moderate staining). Application of the OSDI and the DEWS algorithms resulted in "misclassification," or shifting of subjects, between the dry eye and normal groups.
PURPOSE: Without a single diagnostic test or survey that serves as a "gold standard" test for dry eye and/or meibomian gland dysfunction (MGD), diagnostic algorithms are becoming commonplace in clinical care as well as clinical trials. Inclusion or exclusion of tests in an algorithm is likely to affect prevalence of dry eye or MGD in a practice or in clinical trials. Multiple algorithms are compared, and the weights of individual tests in the algorithms are examined.
METHODS: A full ocular surface evaluation was conducted on 439 postmenopausal women. All subjects signed informed consent prior to enrollment. Diagnostic algorithms, including Delphi (Behrens, 2006), DEWS (2007), OSDI (Schiffman, 2000), and the MGD report (Nichols, 2011) are compared.
CONCLUSIONS: Strict interpretation of algorithms can result in "under diagnosis" when patients do not meet all criteria for a specific category, yet non-specific survey-based classifications create non-homogenous patient groups. Understanding the overlap between groups may streamline diagnoses for clinical care and clinical trials.
ADDITIONAL COMMENTS: Grant support: NEI R01EY015519