Course Description: This lecture discusses several new and unique strategies to address ocular surface disease, including common and atypical forms of blepharitis, keratitis and dry eye. Included are discussions of mechanical therapies for lid disease, unique new therapies for dry eye disease, preserved amniotic membranes and treatments for Demodex.

Learning Objectives/Outcomes: At the conclusion of this course, the attendee will be able to:

1. Describe several new and novel mechanical therapies for anterior and posterior blepharitis;
2. Identify the rationale and indications for using autologous serum eyedrops;
3. Discuss neurostimulation as a treatment modality for dry eye disease;
4. Identify the rationale and indications for the use of preserved amniotic membranes;
5. Appreciate the emerging role of biologic preparations for ocular surface disease.
6. Delineate a variety of treatment options for demodicosis.

WHAT IS OCULAR SURFACE DISEASE?

A. A newer, sexier, more politically-correct term for “dry eye”
B. A severe form of keratoconjunctivitis that involves decompensation of the cornea
C. Any dysfunction involving the integrated structures of the ocular surface

DIAGNOSTIC CONSIDERATIONS IN OCULAR SURFACE DISEASE

- Evaluation MUST include assessment of:
  - Lid margins
  - Blink dynamics
  - Tears (quality and quantity)
  - Corneal integrity
  - Surface “landscape”
• **Primary diagnoses:**

- Lid margin disease (a.k.a. blepharitis, meibomian gland dysfunction)
- Lagophthalmos (a.k.a. blink lagophthalmos or “incomplete blinking”)
- Tear deficiency (a.k.a. “dry eye”)
- Keratoconjunctivitis sicca
- “Topographic disorders”... basement membrane disease, conjunctivochalasis, pinguecula/pterygia
- “Other” surface disease... allergy, infection, toxicity

**CONVENTIONAL THERAPIES OF THE LAST 25 YEARS**

- **Blepharitis**
  - Self-directed eyelid warming, with or without lid massage
  - Self-directed lid cleansing with surfactant cleanser (usually “baby shampoo”)
  - Topical antibiotics or antibiotic/corticosteroid combination therapy
    - erythromycin (Ilotycin®)
    - polymyxin B / neomycin / dexamethasone (Maxitrol®)
    - azithromycin (AzaSite®)
  - Oral/systemic therapy
    - tetracycline-derivatives (e.g. doxycycline)
    - fish oil / omega-3 essential fatty acids

- **Lagophthalmos**
  - “Artificial tears” – drops, sprays, gels, ointments, slow-release pellets (Lacrisert®)
  - “Blink efficiency training”... ?
  - Surgical correction... ?

- **“Dry Eye”**
  - “Artificial tears” – drops, sprays, gels, ointments, slow-release pellets (Lacrisert®)
  - Topical cyclosporine (Restasis®), with or without corticosteroid drops
  - Punctal occlusion (plugs or cautery)

- **K. sicca**
  - “Artificial tears” – drops, sprays, gels, ointments, slow-release pellets (Lacrisert®)
  - Topical cyclosporine (Restasis®), with or without corticosteroid drops
  - Oral secretagogues (pilocarpine, cevimeline)
  - Moist Eye moisture panels (EagleVision™) or swim goggles
  - Bandage contact lenses
  - Tarsorrhaphy
NEW & EMERGING THERAPIES FOR LID MARGIN DISEASE

- **Topical Agents**
  - Hypochlorous solution (Avenova®, HypoChlor®)
  - 4-terpineol (Cliradex®) and tea tree oil (BlephaDex®, Oust® Demodex)

- **Mechanical Treatments**
  - Lid margin debridement
  - Microblepharoexfoliation (BlephEx®)
  - Meibomian gland probing (Maskin® technique)
  - Vectored thermal pulsation therapy (LipiFlow®)
  - Externally-administered, heated gland expression (MiBo ThermoFlo®, iLux™)

NEW & EMERGING THERAPIES FOR TEAR DEFICIENCY

- **Topical Agents**
  - Lifitegrast (Xiidra; Shire)
  - Compounded pharmaceuticals:
    - Autologous serum eye drops (ASED)
    - 5% albumin eye drops
    - 5%-10% N-acetylcysteine eye drops

- **Mechanical Treatments**
  - Neuroelectrical tear stimulation (TrueTear; Allergan)

NEW & EMERGING THERAPIES FOR KERATITIS AND OTHER CORNEAL DISORDERS - Amniotic membrane therapy (AMT)

- **What is it?**

  “The amniotic membrane (AM) is the inner avascular layer of the three-layered foetal membrane. The first therapeutic use of AM was successfully achieved by Davis in 1910 for skin transplantation. Subsequently, the first ocular indication for AM was suggested by de Rotth in 1940 following successful treatment of a chemical burn of the ocular surface. Although use of the membrane for ocular indications continued in the Soviet Union, it was not until Juan Batlle’s report in 1992 that it re-emerged as an important modality of treatment. As of 25 September 2008, there are over 700 peer-reviewed publications for the ocular use of AM highlighting novel increasing indications and therapeutic applications.”

- Amniotic tissue possesses an inherent ability to:
  - Reduce inflammation
  - Promote scarless healing (regenerative healing)
  - Inhibit the angiogenic process
  - Minimize pain
- Mechanism
  - AM epithelium and stroma are endowed with numerous cytokines and growth factors, including:
    - transforming growth factor-β6
    - epidermal growth factor
  - Provides a substrate for epithelial cell migration and attachment

**Ophthalmic indications:**

<table>
<thead>
<tr>
<th>Cornea</th>
<th>Conjunctiva</th>
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<tbody>
<tr>
<td>o Chemical burns</td>
<td>o Chemical burns</td>
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<tr>
<td>o Infectious keratitis (i.e. ulcers)</td>
<td>o Conjunctivochalasis surgery</td>
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<tr>
<td>o Limbal stem cell deficiency</td>
<td>o Glaucoma filtering surgery</td>
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<tr>
<td>o Neurotrophic keratitis</td>
<td>o Pterygium surgery</td>
</tr>
<tr>
<td>o Persistent corneal epithelial defects</td>
<td>o Stevens-Johnson syndrome</td>
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<tr>
<td>o Corneal perforations</td>
<td>o Symblepharon prevention</td>
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<tr>
<td>o Pseudophakic bullous keratopathy</td>
<td>o Tumor excision and reconstruction</td>
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**Types and examples (sutureless variety):**

- Cryopreserved membrane products
  - PROKERA® (BioTissue)
  - PROKERA® Slim, PLUS, & Clear
- Dried or dehydrated products
  - Aril™ (Seed Biotech)
  - AMBIODISK® (IOP Ophthalmics)
  - AmnioTek™-C (ISP Surgical)
  - BioDOptix® (BioD, LLC)
  - ReNovoAT-o™ (RegenMed Group)

**AMT INSERTION & REMOVAL TECHNIQUE – VIDEO EXAMPLES**
BIOLOGIC PREPARATIONS FOR OSD

- Biologics are genetically-engineered proteins which are manufactured in a living system
  - 1st generation agents (e.g. blood plasma, insulin) are obtained directly from humans or animals
  - 2nd & 3rd generation agents employ microorganisms, plant or animal cells to produce proteins derived from human genes in a laboratory setting.
  - Many biologics are produced using recombinant DNA technology – defined as “joining together of DNA molecules from two different species that are inserted into a host organism to produce new genetic combinations”
- “Amniotic fluid”
  - Solution derived from processing of amniotic membrane
  - Formulas:
    - Regener-Eyes (Regenerative Network International)
    - Genesis (Ocular Science)
    - Regenesol (Bio-Tissue / TissueTech)
- Anakinra (Kineret; Amgen Inc.)
  - Recombinant version of human IL-1Ra approved for treatment of RA
  - Topical formulation for ophthalmic use
  - Currently under investigation

DEMODEX BLEPHARITIS (DEMODICOSIS)

- Traditional lid hygiene and antibiotics are insufficient to eradicate Demodex
- Most effective therapy involves direct exposure to toxic oils: e.g. tea tree oil, caraway oil, dill weed oil
  - In-office application (20-50% TTO), followed by AB/CS ung qHS
    - 2-3 applications, 2-3 weeks apart
  - Self-directed daily therapy with T4O lid wipes
    - qD X 4 weeks for mild presentations
    - BID X 4 weeks for more severe presentations
    - Can be used in conjunction with in-office therapy
- Oral ivermectin for recalcitrant cases
  - Two 200-mcg/kg doses given 7 days apart
  - Translation: Give three 3 mg tablets per 100 lbs. body weight as a bolus dose at time of diagnosis, then repeat one week later
- 4% pilocarpine gel has shown some efficacy in clinical trials, but its miticidal activity is low
- 0.01% hypochlorous acid has NOT been shown to have substantial miticidal activity