

Take the Bite Out of the Mite: Managing *Demodex* Blepharitis

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Financial Disclosures

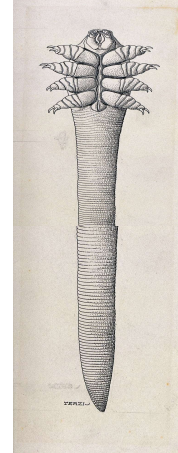
- AbbVie
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What are *Demodex*?

Ectoparasitic mites

- Part of skin's natural microbiome



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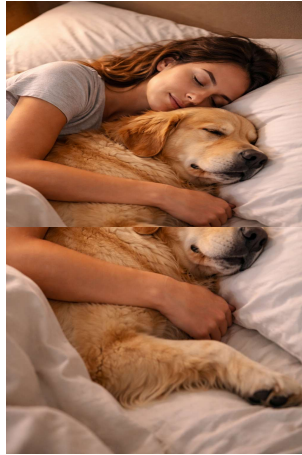
Myth: *Demodex* are (currently) beneficial



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Past: "The enemy of my enemy is my friend"

Myth: You get *Demodex* from your pets



"Don't blame me!"



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Types of *Demodex*

Demodex folliculorum



- 0.3-0.4 mm in length
- Inhabit lash follicles

Demodex brevis



- 0.1-0.3 mm in length
- Inhabit meibomian glands



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Fun fact: Your mites are passed down!



"Thanks, mom!"

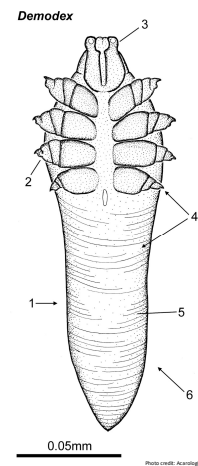


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Demodex Anatomy

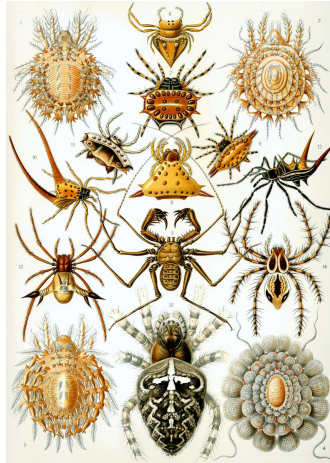
Arthropods

- Cigar-like shaped body
 - Two fused body segments
 - Females shorter and rounder than males
- Exoskeleton
 - Chitinous scales
- Four pairs of legs with clawed ends
 - Grip lashes
- Pincer-like mouth pieces
 - Feed on epithelium



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Fun fact: *Demodex* are arachnids!



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Demodex and Spiders and Ticks, Oh My!

Fun fact: *Demodex* are speed demons!

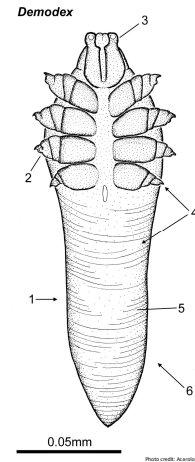


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Demodex have eight, three-muscle-celled legs
that move 8-16 mm/hr

Demodex Physiology

- **Life Cycle**
 - Egg, larva, adult
 - ~3 weeks
- **Lack full digestive system**
 - Feed on epithelial cells and sebum
 - Regurgitate vs defecate
- **Active at night**
 - Feed
 - Mate



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Fun fact: *Demodex* have an anus!



From: Smith G, Manzanera J, et al. Human follicular mites: Ectoparasites becoming symbionts. *Mol Biol Evol*. 2021 Jun 21;38(6):2111-2120. doi: 10.1093/molbev/msab125



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Fun fact: *Demodex* like to party at night!

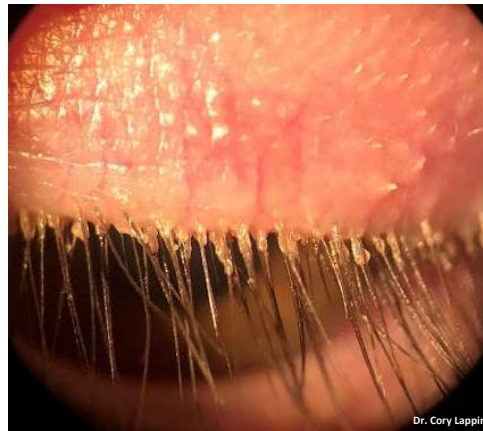


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What is *Demodex* Blepharitis (DB)?

- *Demodex* are part of normal microbiome
- **Overpopulation is thought to be cause of DB**
 - Demodicosis
- **2 million cases of blepharitis in U.S. annually**
 - 69% thought to be caused by DB



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Epidemiology of DB

- **Males and Females**
 - Conflicting data on if male > female, male < female, or no difference
- **All races and ethnicities**
- **All ages**
 - More likely with age



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Epidemiology of DB

DB is common

- 69% of all cases of blepharitis are due to *Demodex* (~2 million cases per year)
- 58% of all eye care patients were shown to have *Demodex* (~25 million patients)



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Epidemiology of DB

Underdiagnosed

- 51% of DB patients had signs and symptoms for four or more years
- 58% never diagnosed with blepharitis
- 33% made at least two visits to ECP for condition
 - 15% made 6 or more



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Epidemiology of DB

Commonly seen alongside other ocular conditions

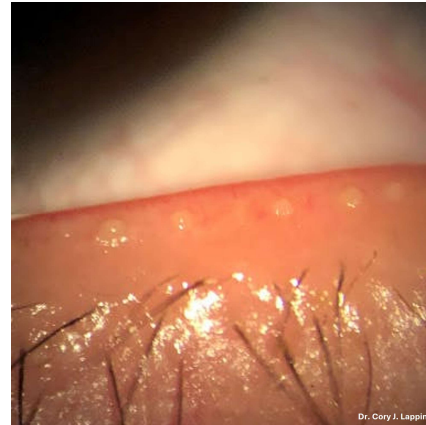
- 65% of glaucoma patients
- 60% of dry eye patients
- 56% of cataract patients
- 51% of contact lens wearers
 - 93% of patients experiencing contact lens intolerance displayed *Demodex*



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Demodex and MGD

- Obstruction and inflammation
- Up to 90% of MGD patients have DB
- 96-99% of patients with moderate to severe DB have MGD
- Consequences:
 - Evaporative dry eye
 - Fluctuating vision



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Risk factors for DB

- **Age**
- **Fair complexion**
 - Rosacea
- **Diet**
- **Environmental**
- **Cosmetic**
 - Artificial lashes
- **Behavioral**
 - Smoking
- **Immunocompromised status**



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Pathophysiology of DB

1. Mechanical

- Microtrauma from physically biting/feeding on epithelial cells
- Physical obstruction of meibomian glands by *D. brevis* (MGD)
- Lash disruption by *D. folliculorum*

2. Chemical

- Release of proinflammatory digestive enzymes

3. Inflammatory

- Chitinous exoskeleton elicits chronic inflammation/hypersensitivity response
- Presence of proinflammatory collarettes

4. Bacterial

- Harbor Staph, Strep, and Bacillus bacteria on/in body

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Symptoms of DB

Relatively nonspecific

- Itching
 - Especially eyelids themselves
- Dryness
- Foreign body sensation
- Watering



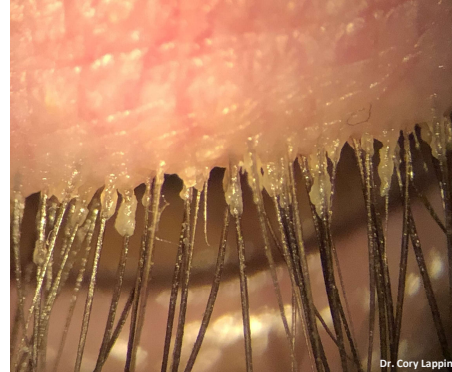
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Diagnosing DB

Collarettes

- Waxy, cylindrical buildup at base of lashes
- Comprised of:
 - Waste
 - Digestive material/enzymes
 - Epithelial cells
 - Keratin
 - Mite eggs
- Pathognomonic for DB
 - ≥ 10 collarettes are present = DB significantly more likely



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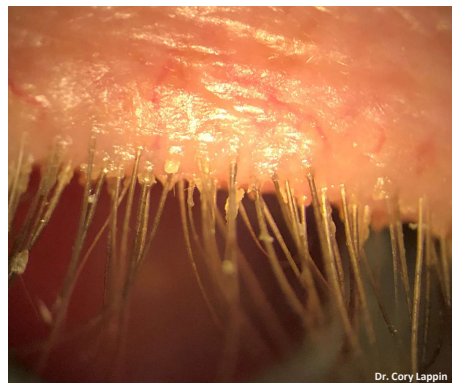


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Diagnosing DB

Diagnostic techniques

- Direct observation with slit lamp
 - Look down
- Mastrota Twirling Technique
- Lash sampling (Coston Method)
 - Epilation + slid preparation
 - Sodium fluorescein, peanut oil, or 75% alcohol
- In vivo confocal laser scanning microscopy (CLSM)

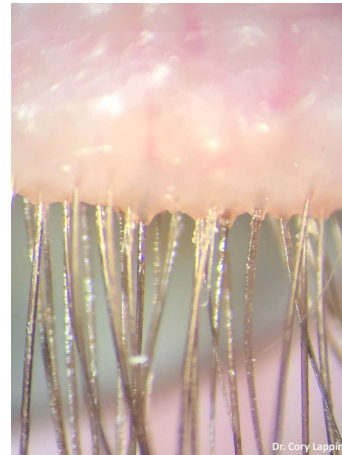
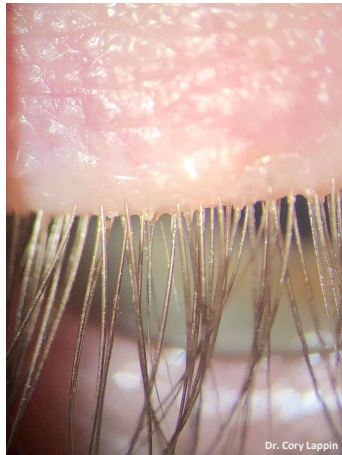
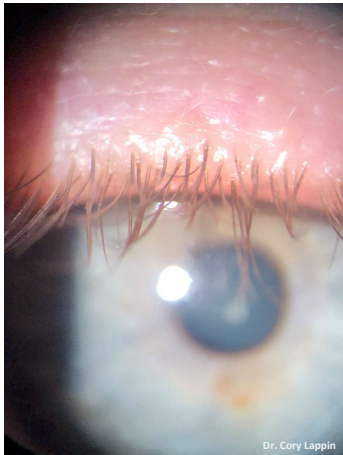


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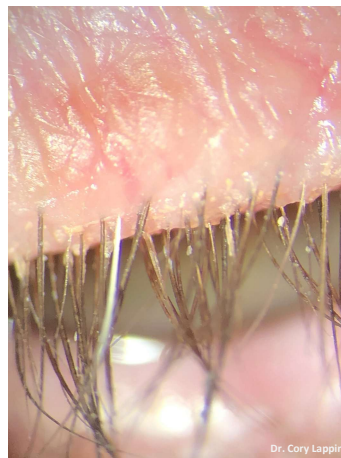
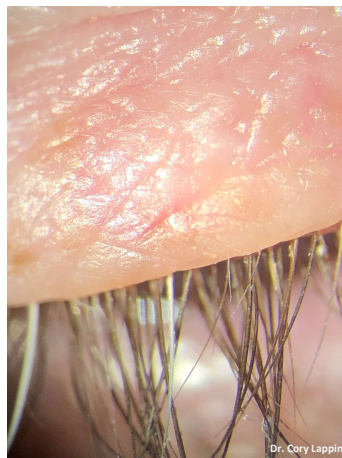
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Why Look Down?



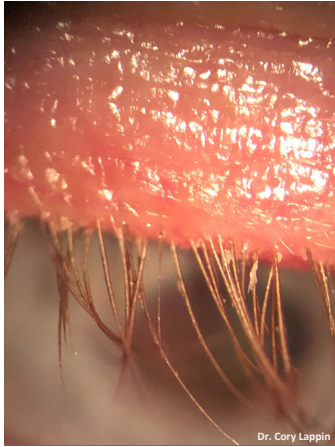
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Fun fact: *Demodex* can hide in the “folds”



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Collarettes



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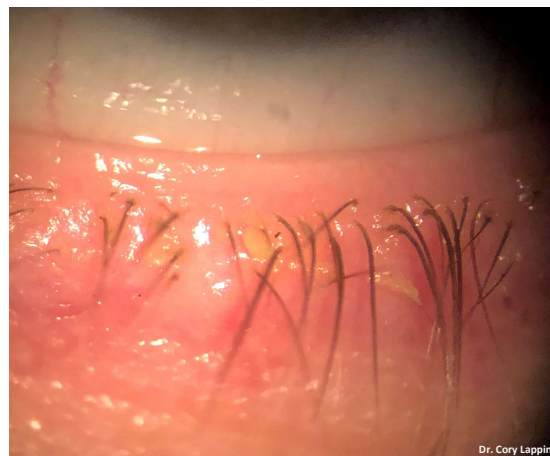


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Lower Lids



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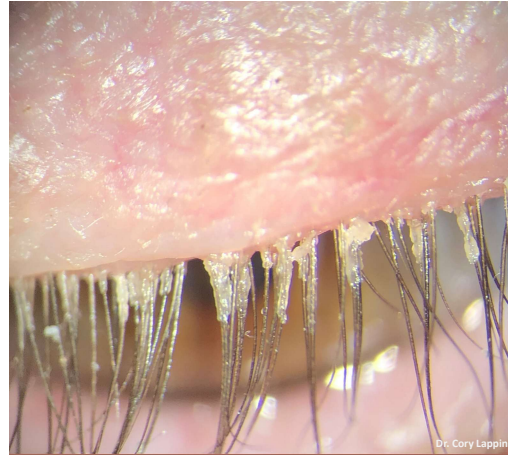


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Manifestations of DB: Lids and Lashes

Blepharitis

- Collarettes
- Lash disruption
 - Madarosis
 - Trichiasis
 - Distichiasis
- Lid margin inflammation
 - Erythema
 - Notching/scarring
 - Thickening
- Meibomian gland obstruction
- Recurrent lid edema

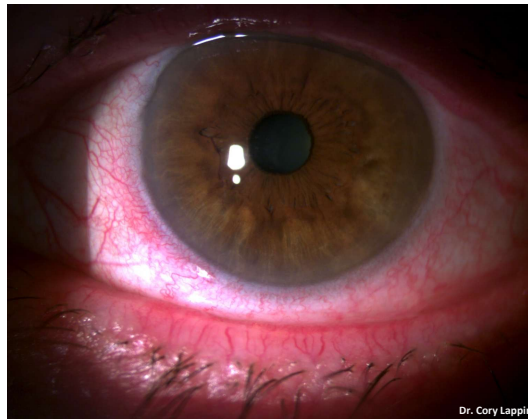


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Manifestations of DB: Conjunctiva

Blepharoconjunctivitis

- Conjunctival injection
- Chemosis

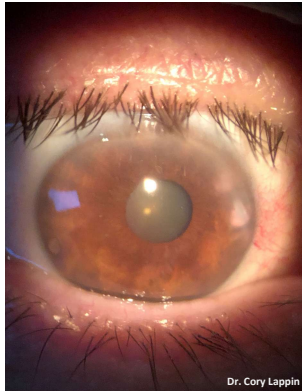


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Manifestations of DB: Cornea

Blepharokeratitis

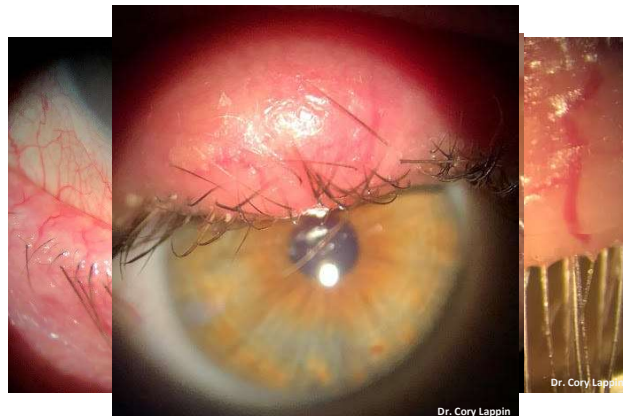
- Neovascularization
- Marginal infiltrates
- Phlyctenules
- Limbitis
- Perforation (rare)



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Comorbidities of DB

- Rosacea
- Meibomian gland dysfunction
- Chalazia
 - Recurrent
- Basal and sebaceous gland carcinoma
- Contact lens discomfort
- Cataracts



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Differential Diagnoses

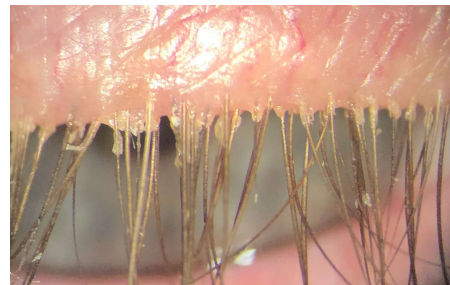
- **Allergies**
 - Itching in both
 - DB tends to affect lids vs eye proper
- **Bacterial blepharitis**
 - Common for both to be present
 - Demodex act as vector for bacteria
 - Saponification vs collarettes
- **MGD**
 - Demodex brevis can physically obstruct glands
 - Demodex associated with altered meibum composition
- **Dry eye**
 - If nonresponsive to traditional treatment, DB should be considered
- **Ocular Rosacea**
 - Common comorbidity, may be interrelated
- **Phthiriasis palpebrarum**
 - Lice infestation of eyelashes
 - Intense itching
 - Bloody – red-brown crusting
- **Herpes keratitis**
 - Nonresponsive to antiviral treatment
 - Common misdiagnosis for Demodex blepharokeratitis



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Differential Diagnoses

- **Allergies**
 - **Bacterial blepharitis**
 - **MGD**
 - **Dry eye**
 - **Ocular Rosacea**
 - **Phthiriasis palpebrarum**
 - **Herpes keratitis**
- Many of these can be concomitant conditions**
- Presence of lash collarettes is the key differentiator



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Impact of DB

Reduction in quality of life

- 80% report negative impact
 - Increased awareness of eyes
 - Difficulty wearing cosmetics
 - Increased hygiene burden
 - Difficulty with nighttime driving



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Treatment of DB

Demodex are highly resistant to most treatments

- Resistant to 75% alcohol and 10% povidone-iodine
- Nonresponsive to antibacterial, antiviral, or antifungal treatment
 - Parasitic arthropods



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Treatment of DB: Lotilaner

Lotilaner ophthalmic solution 0.25% (Xdemvy)

- Antiparasitic agent
- Dosed BID x 6 weeks
 - Two life cycles
- Inhibits parasite-specific GABA-Cl channels
 - Results in paralysis and death of mites
- Penetrates lash follicles and meibomian glands
 - Lipophilic
- First and currently only FDA-approved treatment for DB
 - 60% complete mite eradication (0 mites per lash)
 - 50% complete collarette cure (≤ 2 collarettes on the upper lid)
 - 85% clinically meaningful collarette cure (≤ 10 collarettes on the upper lid)
 - 25% erythema cure
 - **54% improvement in mean number of meibomian glands yielding liquid secretions (MGYLS)**



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Myth: DB is due to poor hygiene



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Treatment of DB: Tea Tree Oil

Active ingredient: Terpinen-4-ol (T4O)

- Antimicrobial and antiseptic with antibacterial, antiviral, antifungal, anti-inflammatory
- Demodicidal
- Acetylcholinesterase inhibitor
- Typically dosed BID x 6 weeks minimum
- TTO vs T4O
 - TTO: higher concentrations and contact time
 - T4O: lower concentrations and contact time
- Relatively harsh
 - ocular irritation, contact dermatitis, and an allergic response

Examples:

- EyeEco's Advanced Formula 2% Tea Tree Eyelid & Facial Cleanser foam (EyeEco)
- Cliradex Light Foam and Towelettes (PRN Vision Group)
- Optase TTO Eye Lid Gel and TTO Lid Wipes (SCOPE)
- Oust Demodex Cleanser foam and Oust Demodex Cleanser Pre-Moistened Pads (OCuSoft)
- Blephadex Eyelid Foam and Blephadex Eyelid Wipes (Blephadex)
- Oust Demodex Swabstix (tea tree oil 50%, OCuSoft)

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Treatment of DB: Hypochlorous Acid

• Antiseptic

- Naturally produced by leukocytes

• Controversial role in DB treatment

- Likely not demodicidal

• Beneficial for bacterial component

Examples:

- HyClear (hypochlorous acid 0.01%, Contamac)
- Avenova (hypochlorous acid 0.01%, NovaBay Pharmaceuticals)
- Optase Protect (hypochlorous acid 0.015%, SCOPE)
- Heyedrate Lid and Lash Cleanser Spray (Hypochlorous Acid 0.015%, PRN Vision Group)

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Treatment of DB: Okra

Okra-based cleansers

- Demodicidal
- Polysaccharide driven mediation of immune response
 - May activate lymphocytes, macrophages, and natural killer cells
- Good for sensitive skin

Examples:

- ZocuFoam Eyelid Cleanser Moisturizer
- ZocuWipe

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Management strategies for DB

Foams vs scrubs

- Foams for routine use
 - Reaches “nooks and crannies”
- Scrubs 2-3x per week
 - Good for removing debris but more abrasive

“Mixed” blepharitis

- Demodex + bacterial blepharitis
 - TTO + HOCl
 - One used in morning, other at night (patient preference)



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Treatment of DB: Debridement

Microblepharoexfoliation

- Remove collarettes and debris
- Remove proinflammatory biofilm
- Uncap obstructed meibomian glands

Examples:

- NuLids PRO (in-office)
- NuLids (at-home)
- ZEST
- BlephEx

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Treatment of DB: Intense Pulsed Light

IPL

- Demodicidal
 - Coagulative necrosis
 - Light energy absorbed by chromophores in exoskeleton
 - **Must avoid lid margin to avoid lash loss**
- Also addresses:
 - MGD
 - Telangiectatic vessels/rosacea
 - Inflammation
 - Bacterial burden



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Treatment of DB: Thermal Pulsation/Expression

- Melts stagnant meibum
- Clears obstruction
- Underlying DB needs to be addressed for maximal benefit

Examples:

- Radiofrequency
- LipiFlow
- iLux
- TearCare

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Treatment of DB: Other Treatments

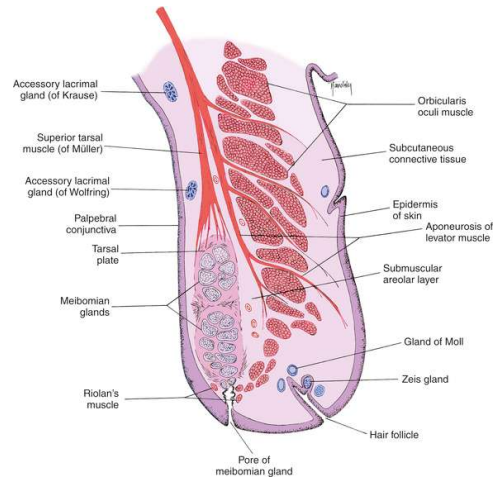
- **Ivermectin**
 - Inhibits Glu-Cl channels
 - Results in paralysis and death of mites
 - Topical and oral
 - Risk of neurological toxicity
- **Metronidazole**
 - Exact mechanism unknown
 - May block synthesis of nucleic acid can cause build of toxic metabolites
 - May help with rosacea
 - Topical and oral
- **Baby shampoo**
 - Ineffective
 - Potentially detrimental



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Myth: You can effectively "smother" *Demodex*



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<https://dme.uh.edu/ocular-adhese-and-lacrimal-system/>

Treatment of DB: Supportive therapies

Foundational treatments:

- **Omega-3 fatty acid supplementation**
 - 3:1 EPA to DHA ratio with at least 2 g of combined EPA and DHA
- **Warm compresses**
- **Lid hygiene**
- **Preservative-free artificial tears**
- **Blink exercise**

Prescription treatments:

- **Immunomodulators**
 - Lifitegrast (Xiidra)
 - Cyclosporine (Cequa, Vevye, Restasis)
- **Neurostimulators**
 - Varenicline (Tyrvaya)
- **Tear film stabilizers**
 - Perfluorohexyloctane (Miebo)



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Management strategies for DB

First line:

- Lotilaner

Maintenance:

- TTO-based cleanser
- Okra-based cleanser
- +/- HOCl cleanser

Heavy lid margin debris:

- Microblepharoexfoliation

Concomitant ocular surface disease:

- Foundational treatments
- IPL
- MGD, rosacea

Dosing and duration:

- BID x 6 weeks for initial Tx
- QD vs every other day for maintenance
- Courses of treatment as needed

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Talking to patients about DB

Education is key

- Emphasize that it is normal to have *Demodex* present
 - Issues occur with overpopulation
- Review symptoms
 - Itching, dryness, FB sensation, watering
 - Recurrent styes
 - Trouble wearing cosmetics or contacts
- Managing symptomatic cases
 - Prescription treatment
 - Maintenance hygiene
 - In-office procedures
- Managing asymptomatic cases
 - Educate and offer
 - "Planting a seed"



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Summary

- **Demodex are ectoparasitic mites that are part of our skin's normal microbiome**
 - DB occurs when *Demodex* overpopulate
- **Blepharitis is one of the most common conditions we encounter as ECPs**
 - 69% of cases are thought to be due to *Demodex*
- **All patients can potentially develop DB regardless of age, race, or sex**
- **DB can have significant negative impact on ocular surface function**
 - 90% of MGD patients have DB and 96-99% of moderate to severe DB patients have MGD
 - 54% improvement in mean number of meibomian glands producing liquid secretion after treatment with lotilaner
- **DB is underdiagnosed but can have significant impact on quality of life**
- **DB is easily diagnosed**
 - Have patient look down, presence of collarettes is pathognomonic for DB



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Summary

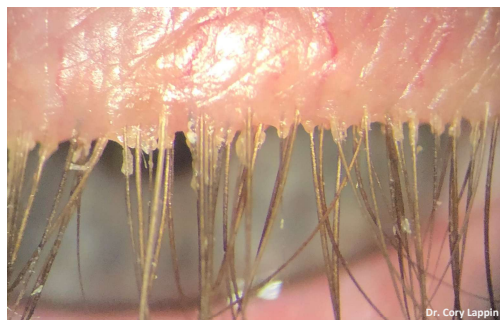
- **DB is easily treated**
 - Rx: Lotilaner ophthalmic solution (Xdemyv)
 - Six-week course of treatment with lotilaner resulted in 85% showing collarette reduction to ≤ 10 collarettes and 60% mite eradication
 - Maintenance Hygiene: TTO, Okra, HOCl
 - Adjunct In-office procedures: Microblepharoexfoliation, IPL
- **Patient education is key to successful treatment**



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Thank you!

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