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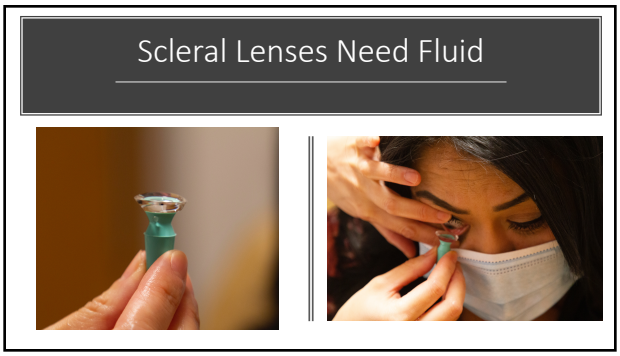


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## Early Scleral Lens Filling Solution

- Not FDA approved
- Used off-label for filling
- Discontinued in 2015


5

## Scleral Lens Filling Solutions

- Off-label:
  - 0.9% NaCl Inhalation saline NB (3, 5, 15 mL)
    - Addipak, Modudose
  - NPATs
- FDA approved
  - PuriLens Plus Saline 120 mL/ 4 oz B (The LifeStyle Company)
    - PuriLens Mini (60 mL/ 2 oz)
  - Lacripure 5 mL NB (Menicon, 2016)
  - ScleralFil 10 mL B (Bausch + Lomb, 2017)
  - NutriFill 10 mL (Contamac)
  - VibrantVue 5 mL NB (VibrantVue)

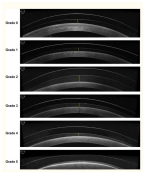





6

## Filling Solutions and Symptoms

- Fogt JS, et al. Changes in Symptoms of Midday Fogging with a Novel Scleral Contact Lens Filling Solution. Optom Vis Sci. 2020. PMID: 32941340
  - Evaluated solution containing:
    - sodium, phosphate, potassium, calcium, and magnesium
  - 22 existing SL wearers, Not masked
  - OSDI scores decreased from 27.1 to 9.1 (p=.006)
  - Current Symptoms Survey showed decreased:
    - Burning/stinging
    - Grittiness/FB sensations
    - Dryness
    - Blur/fluctuating VA
    - Overall pain/discomfort
  - Objective staining/fogging decreases not statistically significant



- Midday fogging may be related to inflammation
  - Presence of different types of particulate matter indicates different mechanisms:
    - solution incompatibility with corneal cells
    - friction or compression from excessive lens movement or rocking
    - overall tightness upon the ocular surface
      - Jennifer Swingle Fogt. Midday Fogging of Scleral Contact Lenses: Current Perspectives. Clin Optom (Auckl). 2021; 13: 209–219.

7

## Do NOT fill scleral lenses with

- Preserved saline
- Preserved artificial tears
- Gas permeable soaking solutions
- SCL Multipurpose solutions
- GP Multipurpose solutions
- Peroxide solutions

- Will lead to surface toxicity


8

## PuriLens Plus

- Multi-dose preservative-free, pH-balanced, sterile saline buffered with boric acid and sodium borate
- **Initial OFF-LABEL for scleral lens use:** part of a PuriLens System developed to clean and disinfect soft hydrophilic contact lenses by **subsonic agitation and UV irradiation** of the storage solution

  **Never intended for scleral lens care and wear**
- FDA approved for Scleral Lens use in 2021


- Human Tear pH: range 6.5-7.6 (avg 7.0)
- **Concentations:**
  - Boric acid: **0.284%** (pH 5.1)
  - Sodium Borate: **0.030%** (pH ~8-9)
  - Sodium Chloride: 0.770%
  - Water for injection: 98.916% (pH 7)
  - Does not contain chlorhexidine, thimerosol or other mercury-containing compounds

9

- **Boric Acid** (hydrogen borate)
  - Antiseptic
  - Insecticide
  - Antifungal
  - Flame retardant
  - Adjunct pH buffer
  - Lubrication
  - Naturally occurring compound in food
  - Eyewash, cure infections (?)



- **Sodium Borate** (borax)
  - Component in detergents, cleaning products, cosmetics
  - Antifungal
  - Fire retardant

10

## Microorganism growth in multi-dose preservative free saline solution commonly used off-label for scleral lens wear

Karen Lee OD, Gloria Chiu OD, Seungheon Lee MD, Rosemary She MD. ARVO May 2018

**Purpose:** Explore the time course of possible microbial contamination of an **unused, uncapped bottle of preservative-free saline solution**

- Saline sampled upon opening and at **1, 2, 7, 30 and 63 days** after opening
- Saline bottle kept at 22-25° C and 25-52% humidity

**Results:** **NO bacterial or fungal growth was detected** in aerobic or anaerobic blood culture media, Standard Methods Agar, or Sabaraud Dextrose Agar up to 63 days

- Baseline for future studies examining preservative free saline used during scleral wear to explore potential contamination of multi-dose saline


11

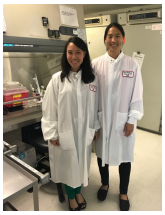
› Optom Vis Sci. 2020 Mar;97(3):162-168. doi: 10.1097/OPX.0000000000001492.

### Bacteriostatic Effect of Multidose Preservative-free Buffered Saline Used in Scleral Lens Wear

Wonjae Seo [1], Gloria B Chiu, Rosemary C She [1]

Affiliations + expand

PMID: 32168238 DOI: 10.1097/OPX.0000000000001492



**Abstract**

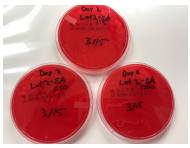
**Significance:** Scleral lenses have become an increasingly common treatment for ocular surface disease and irregular corneas. Multidose, preservative-free saline solutions are frequently used off-label to fill scleral lenses. Because the fluid resides over the ocular surface during lens wear, contaminated solutions may increase the risk of infectious complications.

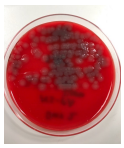
**Purpose:** We sought to assess the viability of skin microorganisms and pathogens associated with keratitis once introduced into a multidose preservative-free saline (MDPFS) solution containing the bacteriostatic agent boric acid (PuriLens Plus; The Lifestyle Co., Inc., Freehold, NJ).

12

## Definitions

- Bacteriostatic
  - agent that stops bacteria from reproducing, while not necessarily killing them
- Bactericidal
  - Agent that kills bacteria





13

## Bacteriostatic Effect of Multidose Preservative-free Buffered Saline Used in Scleral Lens Wear

- Methods
  - Eleven bacterial & one yeast isolate inoculated to 3 lots of MDPFS & sterile normal saline (0.9% NaCl)
    - Based on common organisms causing eye infections and most frequent organisms isolated from specimens at USC Keck hospital
  - Microorganism concentrations enumerated at Baseline & Days 1, 3, 7, 14, 21, 28
  - Persistence of microorganism viability evaluated

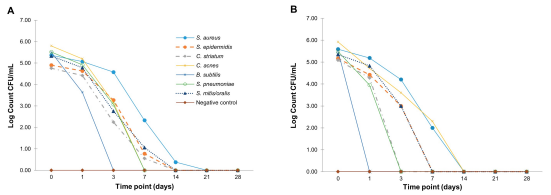
**TABLE 1.** Microorganism strains used in this study and original source of organism isolation

| Microorganism | Origin | Specimen source |
|---|---|---|
| *Staphylococcus aureus* (methicillin-sensitive) | Clinical | Wound |
| *Staphylococcus epidermidis* | Clinical | Wound |
| *Streptococcus pneumoniae* | Clinical | Wound |
| *Streptococcus mitis/oralis* | Clinical | Blood |
| *Corynebacterium striatum* | Clinical | Wound |
| *Cutibacterium acnes* | Clinical | Wound |
| *Bacillus subtilis* NRS-231 (ATCC 6633) | Type strain | N/A |
| *Pseudomonas aeruginosa* | Clinical | Respiratory |
| *Escherichia coli* | Clinical | Wound |
| *Achromobacter xylosoxidans* | Clinical | Urine |
| *Moraxella catarrhalis* | Clinical | Respiratory |
| *Candida albicans* | Clinical | Wound |

N/A = not applicable.

14

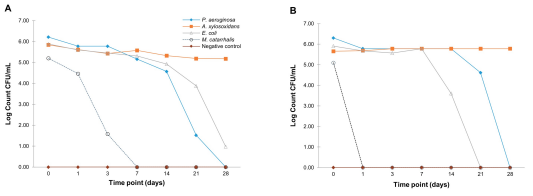
## Bacteriostatic Effect of Multidose Preservative-free Buffered Saline Used in Scleral Lens Wear




Changes in **gram-positive bacteria** concentrations during the 28-day period after inoculation to MDPFS (A), with each value representing mean results from 3 different PuriLens MDPFS lots, and normal saline (B).
CFU = colony-forming unit

15

## Bacteriostatic Effect of Multidose Preservative-free Buffered Saline Used in Scleral Lens Wear



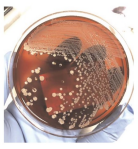

Changes in **gram-negative bacteria** concentrations during 28-day period after inoculation to MDPFS (A), with each value representing mean results from 3 different PuriLens MDPFS lots, and normal saline (B).
CFU = colony-forming unit

16

## **Conclusions:** Bacteriostatic Effect of Multidose Preservative-free Buffered Saline Used in Scleral Lens Wear

- Persistence of organism viability was similar in PuriLens Plus and normal saline (0.9% NaCl)
- Multidose preservative-free saline solution showed bacteriostatic effect for all microorganisms included in the study
  - But, lacked antimicrobial effectiveness against the persistence of viability of **E. coli, P. aeruginosa, or A. xylosoxidans**
  - Achromobacter xylosoxidans and P. aeruginosa known for intrinsic abilities to survive disinfectants and to form biofilm, including those on contact lenses
  - Gram-positive organisms showed shorter viability than gram-negative organisms tested
  - Reduction of Candida alibcans (yeast) was not achieved in normal saline
- Take-away:
  - Enteric and environmental gram-negative organisms, many of which can contribute to infectious keratitis, can persist for weeks once introduced into saline solutions

17



› Optom Vis Sci. 2021 Mar 1;98(3):250-257. doi: 10.1097/OPX.0000000000001657.

### Microbiological Evaluation of Opened Saline Bottles for Scleral Lens Use and Hygiene Habits of Scleral Lens Patients

Moon Jeong [1], Karen L Lee [2], Rosemary C She [1], Gloria B Chiu

Affiliations + expand

PMID: 33771954 DOI: 10.1097/OPX.0000000000001657

**Abstract**

**Significance:** Scleral lenses have become a widely used treatment option for patients with irregular corneas and ocular surface disease. Successful wear entails use of a nonpreserved saline solution to fill the lens before application on the eye.

**Purpose:** The purposes of this study were to evaluate solution from opened bottles of multidose preservative-free saline for microbiological growth and to better understand study participant hygiene habits while handling these bottles for scleral lens wear.

18

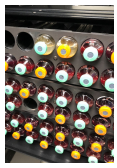
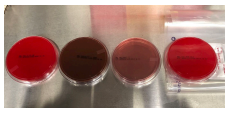
## Methods

- Single-center, prospective study at the Keck School of Medicine of the USC, Department of Ophthalmology
- Eligible subjects were scleral lens wearing patients
  - Used Purilens for scleral lens rinsing and filling
  - Asked to submit their current opened bottle for new one
    - Had at least 15 mL remaining
  - Bottles collected between July – October 2018
    - Submitted for evaluation within 4 hours
  - Subjects completed 12 question survey regarding hygiene habits
- Study Approved by USC IRB (IRB # HS-18-00352)

19

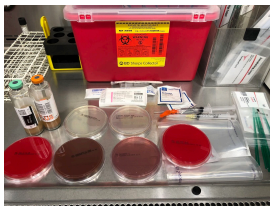
## Methods

- Saline bottles processed by USC microbiology lab
  - Bacterial & fungal cultures within 28 hrs of collection
    - 3.5 – 5 mL saline inoculated into each aerobic & anaerobic blood culture bottle
    - Incubated on BacT/ALERT 3D system for 5 days
    - Also plated 1 mL on:
      - SMA (Standard Methods Agar; **non-selective growth**)
      - SDA (Sabouraud dextrose agar; **fungi**)

20

## Overall Set-up and Supplies



**Culture Media**

Support growth for different organisms

- Sabouraud Dextrose Agar (light yellow)
- Standard Methods Agar (light yellow)
- Blood Agar 5% sheep blood (Red)
- Chocolate Agar (Milk Brown)
- MacConkey Agar (light Pink)
- Anaerobic Blood Agar (Red)

21

## Microbial Growth

22

## Organism Identification

Matrix-Assisted Laser Desorption Ionization Time-Of-Flight (MALDI-TOF) mass spectrometry (Vitek MS, bioMérieux)


23

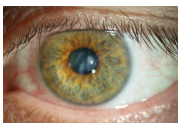
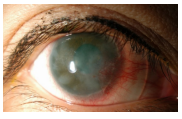
## Results

Data collected from 35 subjects
- Ages 6 – 81 (avg 47.9 +/- 18) years
- 19 (54.3%) Male, 16 Female

**TABLE 1.** Types of ocular conditions in study participants

| Irregular corneas | n = 19 | Ocular surface disease | n = 16 |
|---|---|---|---|
| Keratoconus | 13 | Stevens-Johnson syndrome | 4 |
| Post–penetrating keratoplasty | 3 | Ocular graft versus host disease | 6 |
| Post-LASIK ectasia | 1 | OCP/MMP | 2 |
| Other ectasia | 1 | Sjögrens syndrome | 2 |
| Corneal scar | 1 | Other dry eye syndrome | 2 |

LASIK = laser-assisted *in situ* keratomileusis; MMP = mucus membrane pemphigoid; OCP = ocular cicatricial pemphigoid.

24

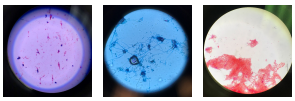
## Results

- **Overall rate of microbial contamination** among saline samples was **62.9%** (n=22)
- **21 different microorganisms identified**
  - Gram-positive (n=26, 56.5%) and Gram-negative (n=20, 43.5%) bacteria
- 22 samples with microorganism growth
  - 12 (54.5%) were polymicrobial and 10 (45.5%) were monomicrobial
- No fungi were recovered

25

## Organisms Cultured

- **Gram Positive (n=26)**
- **7 distinct**
  - Staphylococcus warneri (8)
  - Staphylococcus epidermidis (9)
  - Staphylococcus pasteuri (4)
  - Staphylococcus haemolyticus (2)
  - Kocuria kristinae (1)
  - Micrococcus luteus (1)
  - Diphtheroid (1)



- **Gram Negative (n=20)**
- **14 distinct**
  - Klebsiella pneumonia (2)
  - Klebsiella oxytoca (2)
  - Enterobacter aerogenes (1)
  - Enterobacter cloacae complex (1)
  - Pseudomonas aeruginosa (1)
  - Pseudomonas fluorescens (2)
  - Serratia marcescens (3)
  - Citrobacter freundii (1)
  - Acinetobacter ursingii (2)
  - Delftia acidovorans (1)
  - Pluralibacter gergoviae (1)
  - Ochrobactrum anthropic (1)
  - Stenotrophomonas maltophilia (1)
  - Escherichia coli (1)

26

## Positive Culture = Infection?

- Retrospective review of 35 subjects
  - **No** documented case of Microbial Keratitis (MK)
  - Period of chart review ranged from 11 to 48 months (mean 29.7 months)
  - Ocular complications
    - Subject 5 (SJS) M — Pseudomembranous conjunctivitis
    - Subject 7 (SJS) M — Bacterial conjunctivitis
    - Subject 22 (KC) F — Bacterial conjunctivitis
  - These 3 subjects all **had NEGATIVE cultures**

27

## Survey Questions

Score Legend: 4 = All of the time, 3 = Most of the time, 2 = Half of the time, 1 = Some of the time, 0 = None of the time

1. How often does the **tip of your saline bottle touch your scleral lens plunger** (application or removal)?
2. How often does the tip of your saline bottle **touch your scleral lens** (during filling, during rinse, or other time)?
3. How often does the tip of your saline bottle **touch your eyelid or eyelashes**?
4. How often does the tip of your saline bottle **touch your hand or fingers**?
5. How often do you **recap your saline bottle** after each use?
6. How often do you leave your opened (capped or uncapped) saline bottle in a potentially **warm/hot environment** (car, sun)?
7. How often do you **wash your hands** immediately before handling your saline bottle? 7a. If so, how often do you **use soap** when washing your hands before handling the saline bottle?
8. How many minutes do you **leave the cap off** the saline bottle during an application or removal session?
9. How often do you **replace your saline bottle** after opening (in days)?
10. Do you **carry your saline bottle** with you all day? 10a. If yes, in **what fashion** (pocket, purse, separate pouch, backpack)?
11. Do you keep **multiple bottles open** at a time (bathroom, office, car, etc)?
12. How many **days ago did you open** this saline bottle (one giving up for study)?

28

## Survey Results (Self-reported)

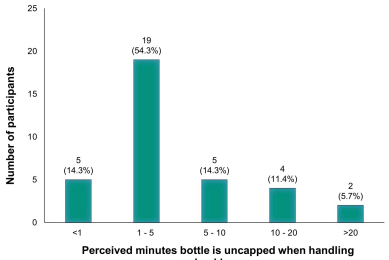
| | All of the time | Most | Half | Some | None |
|---|---|---|---|---|---|
| **How often does the tip of your saline bottle touch your...** | | | | | |
| 1. scleral lens plunger (application or removal)? | 0.00% | 2.86% (1) | 5.71% (2) | 28.57% (10) | 34.29% (12) |
| 2. scleral lens (during filling, during rinse, or other time)? | 0.00% | 5.71% (2) | 5.71% (2) | 14.29% (5) | 74.29% (26) |
| 3. eyelid or eyelashes? | 2.86% (1) | 0.00% | 5.71% (2) | 25.71% (9) | 65.71% (23) |
| 4. hand or fingers? | 2.86% (1) | 2.86% (1) | 0.00% | 37.14% (13) | 57.14% (20) |
| **How often do you...** | | | | | |
| 5. recap your saline bottle after each use? | 97.14% (34) | 2.86% (1) | 0.00% | 0.00% | 0.00% |
| 6. leave your opened saline bottle in a potentially warm/hot environment? | 0.00% | 0.00% | 8.57% (3) | 51.43% (18) | 40.00% (14) |
| 7. wash your hands immediately before handling your saline bottle? | 82.86 (29) | 11.43% (4) | 2.86% (1) | 2.86% (1) | 0.00% |
| 7a. use soap when washing your hands before handling the saline bottle? | 91.43% (32) | 2.86% (1) | 0.00% | 5.71% (2) | 0.00% |

51.4% (n = 18) reported carrying saline bottle around all day
Most carried in a separate pouch (31.4%; n = 11), 1 in a purse, 2 in backpack, 1 in a fanny pack, and 3 in pocket

Most study participants (65.7%, n = 23) reported only opening up one bottle at a time

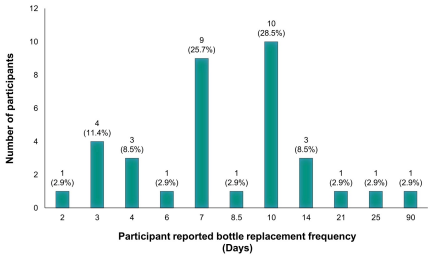
29

## Length of time bottle uncapped during handling



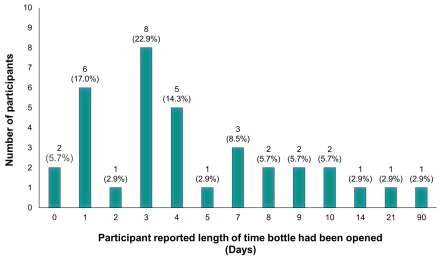

30

## Participant-reported saline bottle replacement frequency




31

## Number of days specimen bottle opened before collection




32

## Ocular Surface Disease vs. Irregular Cornea

| | OSD | % | Irregular K | % | p-value (Fisher exact test) |
|---|---|---|---|---|---|
| Culture w/ any growth | 10/16 | 62.5% | 12/19 | 63.2% | 1.00 |
| Growth of Gram-negative | 2/16 | 13% | 6/19 | 32% | 0.244 |
| Growth of Gram-positive | 8/16 | 50% | 9/19 | 47% | 1.00 |
| Growth of 2+ organisms | 3/16 | 19% | 10/19 | 53% | 0.152 |

No significant difference in cultures due to category of ocular condition (P > .999)
No significant difference in growth of gram-positive (P > .999) and gram-negative organisms (P > .999) or in growth of two or more organisms (P = .15) based on category of ocular condition

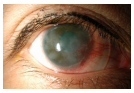
33

## Results

- Survey responses did not differ significantly (P > .05) for the 12 questions with regards to likelihood of positive culture
- No significant age or sex differences between participants with positive and negative culture results
- No significant differences between specific microorganism isolation and survey responses

34

## Clinical Pearls

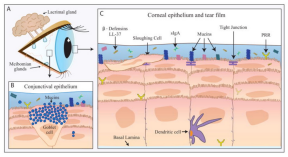


- Scleral lens patients have complex OSD & corneal conditions
  - Fluid is required to fill chamber below lens
- Many PF options to fill chamber
  - Single use and multi-dose
  - FDA approved and Off-Label
- Considerations:
  - Cost, Environmental waste, Travel frequency, Hygiene
- Multi-dose bottles **may** become contaminated during use
  - Doctors and patients need to be aware of possible contaminations that MAY increase risk of ocular complications
- Microbial presence does not mean adverse ocular complication will arise
  - Natural bacteria flora on lids, lashes, skin

35

## Ocular Surface Protective Mechanisms

- Eyelids
- Eye lashes
- Conjunctival mucus membrane
- Corneal epithelial cell tight junctions
- Secreted enzymes
- Mucins
- Tear film layer
- Tear antimicrobial components
  - Immunoglobulins
  - Lysozymes
  - Lactoferrin
  - Surfactant protein-D



Innate immune system of the ocular surface.

The innate immune system is the first line of defense against invasion for the ocular surface (A) and includes components of the conjunctival (B) and corneal epithelium and tear film (C). PRR=pattern recognition receptors, LL-37= cathelicidin, sIgA=secretory Immunoglobulin A

Narayanan S, Redfern RL, Miller WL, et al. Dry Eye Disease and Microbial Keratitis: Is There a Connection? Ocul Surf 2013;11:75–92.
McDermott AM. Antimicrobial Compounds in Tears. Exp Eye Res 2013;117:53–61.

36

## Contact Lens Related Microbial Keratitis (MK) Incidence

- Incidence of CL-related microbial keratitis:
  - 2–4 per 10,000 wearers per year for daily soft lens wearers
  - 20 per 10,000 for overnight soft lens wearers
    - Carnt N, Samarawickrama C, White A, Stapleton F. The diagnosis and management of contact lens-related microbial keratitis. Clin Exp Optom. 2017 Sep;100(5):482-493.
- CL-related microbial keratitis presenting in Australia over a 12-month period
  - DW RGP wearers, annualized incidence per 10,000 wearers was 1.2
  - DW soft CL wearers 1.9
  - Soft CL wearers (occasional overnight use) 2.2
  - Daily disposable CL wearers 2.0
  - Daily disposable CL wearers (occasional overnight use) 4.2
  - DW silicone hydrogel CL wearers 11.9
  - Silicone hydrogel CL wearers (occasional overnight use) 5.5
  - Overnight wear soft CL wearers 19.5
  - Overnight wear of silicone hydrogel 25.4
    - Stapleton F, et al. The incidence of contact lens-related microbial keratitis in Australia. Ophthalmology. 2008.

37

## Risk Factors for Complications

https://eyewiki.aao.org/Acanthamoeba_Keratitis

- Significant risk factors for Acanthamoeba keratitis:
  - Wearing lenses for orthokeratology
  - Sleeping while wearing lenses
  - Storing lenses in tap water
  - Topping off solution in case
    - Cope JR, Collier SA, Schein OD, Brown AC, Verani JR, Gallen R, Beach MJ, Yoder JS. Acanthamoeba Keratitis among Rigid Gas Permeable Contact Lens Wearers in the United States, 2005 through 2011. Ophthalmology. 2016 Jul;123(7):1435-41.
- Risk factors associated with the greatest increased odds of CL-related MK:
  - Using disinfecting solution more than 3 months (odds ratio[OR]1/41.94)
  - Cosmetic CL wear and use of multipurpose disinfection solution (1.37 each)
  - Overnight wear, and soft lens use (OR1/41.24 each)
  - Protective factors associated with the greatest reduction in OR
    - Fitting by an ophthalmologist (OR1/40.73) and hyperopia versus myopia (OR1/40.75)
    - Sauer A, et al. Risk Factors for Contact Lens-Related Microbial Keratitis: A Case-Control Multicenter Study. Eye Contact Lens. 2016.

38

## Scleral Lens Wear and Infectious Risk

- Protective?
  - Acts as barrier and relieves symptoms in OSD
  - Role in healing for persistent epithelial defects
    - Khan M, Manuel K, Vegas B, Yadav S, Hemmati R, Al-Mohtaseb Z. Case series: Extended wear of rigid gas permeable scleral contact lenses for the treatment of persistent corneal epithelial defects. Cont Lens Anterior Eye. 2019 Feb;42(1):117-122.
  - Mechanism for drug delivery
    - Lim P, Ridges R, Jacobs DS, et al. Treatment of Persistent Corneal Epithelial Defect with Overnight Wear of a Prosthetic Device for the Ocular Surface. Am J Ophthalmol 2013;156:1095–101.
    - Paul S, Natarajan R, Iqbal A. Prosthetic Replacement of Ocular Surface Ecosystem Scleral Lens: Benefits of an In-Clinic Therapeutic Approach for Persistent Corneal Epithelial Defect. Eye Contact Lens. 2021 Oct 1;47(10):578-580.
- Risk for infection?
  - Similar to SCL or RGP wear?
- Limited published literature on microbial keratitis (MK) from scleral lens wear

39

## Thank You!

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40