Contact Lenses and Corneal Infiltrates: From Tissue to Treatment

<table>
<thead>
<tr>
<th>Format</th>
<th>Category: Contact Lenses</th>
<th>Total CE Hours: 1</th>
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<tbody>
<tr>
<td>Description:</td>
<td>Contact lens associated corneal inflammatory events (CIEs) are discussed with incidence rates for extended wear provided. Clinical etiologies are presented which challenge the traditional &quot;sterile&quot; keratitis approach. Risk factors and innate immune response leading to these CIEs will be covered, and based on the risk factors, treatment and prevention will be provided.</td>
<td></td>
</tr>
<tr>
<td>CEE:</td>
<td>No</td>
<td>Expires: Course Expires: 07/12/2015</td>
</tr>
<tr>
<td>Instructor:</td>
<td>Loretta Szczotka-Flynn O.D.</td>
<td></td>
</tr>
<tr>
<td>Co-instructors:</td>
<td></td>
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<td>Learning Objectives:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Understand the incidence of contact lens induced corneal infiltrates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Understand risk factors for contact lens corneal infiltrates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Understand the pathophysiology of lens bioburden on corneal infiltrates</td>
<td></td>
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</tr>
</tbody>
</table>
Contact Lens Related Corneal Infiltrates: From Tissue to Treatment

LORETTA SZCZOTKA-FLYNN OD, PhD, FAAO(dipl CL)

Professor
Case Western Reserve University
Department of Ophthalmology & Visual Sciences
University Hospitals Eye Institute

Recent Disclosures: Vistakon, Alcon, Bausch & Lomb

The Epidemiological Perspective

*cartoons taken from Epidemiology, 3rd Edition by Leon Gordis*
### Annualized incidence of MK in the pre-silicone hydrogel era

<table>
<thead>
<tr>
<th>Study Region</th>
<th>Year</th>
<th>Lens Type</th>
<th>Annualized incidence per 10,000 wearers</th>
<th>95% CI Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>New England</td>
<td>1999</td>
<td>Conventional Low Dk</td>
<td>4.1 (95% CI 3.2-5.2)</td>
<td>3.7 (95% CI 3.1-4.7)</td>
</tr>
<tr>
<td>Holland</td>
<td>1999</td>
<td>Conventional and Disposable Low Dk</td>
<td>3.6 (95% CI 3.0-4.5)</td>
<td>2.6 (95% CI 2.3-3.0)</td>
</tr>
<tr>
<td>West of Scotland</td>
<td>1999</td>
<td>Conventional and Disposable Low Dk</td>
<td>2.1 (95% CI 1.6-2.7)</td>
<td>Not available</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>New England</td>
<td>2000</td>
<td>Conventional Low Dk</td>
<td>20.0 (95% CI 15.1-26.7)</td>
<td>3.5 (95% CI 2.7-4.5)</td>
</tr>
<tr>
<td>Holland</td>
<td>2000</td>
<td>Conventional and Disposable Low Dk</td>
<td>20.9 (95% CI 15.1-26.7)</td>
<td>4.1 (95% CI 3.0-5.2)</td>
</tr>
<tr>
<td>New England</td>
<td>1989</td>
<td>Low Dk</td>
<td>25.4 (95% CI 20.3-32.0)</td>
<td>Not available</td>
</tr>
</tbody>
</table>

**Annualized Incidence per 10,000 wearers:**
- **1 in 2500**
- **1 in 500**

### Annualized incidence of MK in the Silicone Hydrogel era

- **Schein et al 2005 Ophthalmology**
  - 18 per 10,000
  - lotrafilcon A 30 day continuous wear
- **Stapleton et al 2008 Ophthalmology**
  - 11.9 per 10,000  SH daily wear
  - 25.4 per 10,000  SH extended wear

### Dart Case Control Study

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Relative Risk</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Planned Replacement Soft</td>
<td>REFERENCE</td>
<td></td>
</tr>
<tr>
<td>SI-Hy</td>
<td>1.16</td>
<td>0.525</td>
</tr>
<tr>
<td>Other soft</td>
<td>0.87</td>
<td>0.698</td>
</tr>
<tr>
<td>Daily Disposable</td>
<td>1.56</td>
<td>0.009</td>
</tr>
<tr>
<td>RGP</td>
<td>0.16</td>
<td>&lt;0.001</td>
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<th>Risk Factor</th>
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<tbody>
<tr>
<td>Planned (Referent)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Replacement Soft</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Si-Hy</td>
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</tr>
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Defining Infiltrates

- By Etiology
  - Sweeney et al
  - Infectious (microbial keratitis)
  - Non-Infectious
    - CLARE
    - CLPU
    - IK
    - AIK
    - AI

CONTACT LENS ACUTE RED EYE (CLARE)

- Inflammatory reaction of the cornea after overnight wear
- Generalized redness and pain upon awakening
- Usually unilateral
- No corneal stain overlying infiltrates
- Has been associated with high levels of Gram negative bacteria on lens
  - Pseudomonas aeruginosa
  - Serratia marcescens
  - Haemophilus influenzae
- Has also been associated with Gram + Streptococcus pneumoniae
CONTACT LENS
PERIPHERAL ULCER (CLPU)
- Acute inflammatory reaction with PMN infiltration
- Biopsies can be sterile or levels Gm +
- Usually located in corneal periphery
- May be asymptomatic
- Always scar
- Usually adherence of Gram + organisms on lens
  - Associated with S. aureus bacteria
Infiltrative keratitis (IK)
- Diffuse corneal infiltration
- Associated with
  - Pseudomonas aeruginosa
  - Serratia marcescens
  - Haemophilus influenzae
    - Often from nasopharynx

Defining Infiltrates as a continuum of disease severity

Efron & Morgan (2005)
- 10 signs & symptoms (ex. redness, infiltrate size and shape, haze, discomfort, etc.)
- Score range 2-22
  - Adapted version 25 max
  - if > 8: Severe keratitis (MK)

Schein et al (2005)
- Levels 1 & 2
  - Probably MK
- Levels 3-4
  - Infiltrative keratitis
- Level 5
  - Infiltrates not CL related
<table>
<thead>
<tr>
<th>Parameter</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td>None</td>
<td>Mild</td>
<td>Moderate</td>
<td>Severe</td>
<td></td>
</tr>
<tr>
<td>Lid Swelling</td>
<td>Absent</td>
<td>Present</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conjunctival Redness</td>
<td>Absent</td>
<td>Localized</td>
<td>Generalized</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infiltrate Shape</td>
<td>Round</td>
<td>1-2 dots</td>
<td>Irregular</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infiltrate Size (largest)</td>
<td>&lt;=1 mm</td>
<td>1.0-2.0 mm</td>
<td>&gt;=2.0 mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of Infiltrates</td>
<td>1-4</td>
<td>5-10</td>
<td>&gt;10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluorescein Staining</td>
<td>Absent</td>
<td>Present</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surrounding Cornea</td>
<td>Clear</td>
<td>Slight haze</td>
<td>Severe haze</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endothelial Debris</td>
<td>Absent</td>
<td>Present</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypopyon</td>
<td>Absent</td>
<td>Present</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Effect of Lens Discontinuation</td>
<td>Resolving</td>
<td>No change</td>
<td>Slight worsening</td>
<td>Significant worsening</td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Risk (Incidence) of CIE (“significant CIE”)**

<table>
<thead>
<tr>
<th>Lens</th>
<th>Daily Wear (persons)</th>
<th>Extended Wear (eyes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Dk</td>
<td>0.14%</td>
<td>1-2%</td>
</tr>
<tr>
<td>Silicone Hydrogel</td>
<td>0.6%</td>
<td>3-4%</td>
</tr>
</tbody>
</table>

**Significant CIE**

These are all SERIOUS and SIGNIFICANT INFILTRATIVE EVENTS OR THOSE THAT PRESENTED TO A HOSPITAL OR CLINICIAN FOR TREATMENT
“Asymptomatic Infiltrates”

Does Definition Matter?

- Should we worry about asymptomatic or less severe infiltrates?
- Are low grade contact lens associated infiltrates different from those seen in spectacle wearers?
- Are mechanisms different compared to significant infiltrates?
- Is the up-regulation of the host defense system something we should ignore?
- Can asymptomatic infiltrates turn symptomatic if not treated?

Risk (Incidence) of CIE (all grades)

<table>
<thead>
<tr>
<th></th>
<th>Daily Wear (persons)</th>
<th>Extended Wear (eyes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Dk</td>
<td>NA</td>
<td>7%</td>
</tr>
<tr>
<td>Silicone Hydrogel</td>
<td>3-6%</td>
<td>14%</td>
</tr>
</tbody>
</table>
WHAT'S THE RELATIVE RISK?
The Silicone Hydrogel Effect

- Meta Analysis: Key, randomized studies driving the effect

<table>
<thead>
<tr>
<th>Study</th>
<th>Risk Ratio for SH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>2.18 (1.48, 3.19)**</td>
</tr>
<tr>
<td>Bausch &amp; Lomb US FDA</td>
<td>2.16 (1.24, 3.76)*</td>
</tr>
<tr>
<td>Brennan et al</td>
<td>2.18 (1.08, 4.42)*</td>
</tr>
<tr>
<td>Ciba US FDA</td>
<td>1.90 (1.36, 2.66)*</td>
</tr>
<tr>
<td>Fonn et al</td>
<td>2.18 (0.31, 15.27)</td>
</tr>
<tr>
<td>Vistakon US FDA</td>
<td>2.18 (1.52, 3.13)*</td>
</tr>
</tbody>
</table>

*significant at p<0.05  **significant at p<0.005
Confounding

- Almost all SH studies used SH lenses worn for 30 days CW
- Almost all low Dk studies used lenses worn for 7 days EW

Other studies documenting a silicone hydrogel effect during DW or EW

- Radford et al UK Case Control Study 2009
  - 877 Cases with non-ulcerative complications
  - 1069 hospital and 639 population controls
  - Si-Hy increased risk for sterile keratitis
    - INDEPENDENT FROM MODE OF WEAR
    - 2.0 X
  - Si-Hy also associated with
    - Mechanical disorders
      - 1.8 X
    - Attendance with any non-ulcerative complication
      - 1.9 X

Other studies documenting a silicone hydrogel effect on CIEs

- Chalmers et al OVS 2010
  - 1276 soft lens wearers, retrospective chart review
  - Silicone hydrogel lenses increased risk of inflammatory events
    - Hydrogel lenses were protective (0.77 RR)
    - Controlled for mode of wear
Other studies documenting a silicone hydrogel effect on CIEs

- Chalmers et al IOVS 2011
  - CLAY Study
  - 3549 soft lens wearers, retrospective chart review
    - 187 CIEs in 168 patients
  - Silicone hydrogel lenses increased risk of inflammatory events
    - 1.85X
    - Controlled for mode of wear

- Chalmers et al OVS 2012
  - Case Control Study
  - 166 patients with symptomatic CIEs
  - Silicone hydrogel increased risk of CIE
    - 1.99X
  - Daily Wear
    - Extended wear did not find SH to increase risk

Morgan & Efron Study
Annualized Incidence of CIE per 10,000 wearers

<table>
<thead>
<tr>
<th>DW</th>
<th>Non-severe</th>
<th>Severe</th>
<th>RR Non-severe</th>
<th>RR Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>RGP</td>
<td>5.7</td>
<td>2.9</td>
<td>0.4</td>
<td>0.5</td>
</tr>
<tr>
<td>DD</td>
<td>9.1</td>
<td>4.9</td>
<td>0.7</td>
<td>0.8</td>
</tr>
<tr>
<td>Hydrogel</td>
<td>14.1</td>
<td>6.4</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>SH</td>
<td>55.9</td>
<td>0</td>
<td>4.0</td>
<td>Na</td>
</tr>
<tr>
<td>EW</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RGP</td>
<td>0</td>
<td>0</td>
<td>Na</td>
<td>Na</td>
</tr>
<tr>
<td>Hydrogel</td>
<td>48.2</td>
<td>96.4</td>
<td>3.4 (ns)</td>
<td>10.2</td>
</tr>
<tr>
<td>SH</td>
<td>98.8</td>
<td>19.8</td>
<td>7.0</td>
<td>2.1 (ns)</td>
</tr>
</tbody>
</table>
1. ↓ Epithelial permeability
   - Lin, Polse, et al
2. ↓ Bacterial adherence
   - Ren, Cavanagh et al
3. ↓ Microcysts
   - Sweeney and others
4. ↓ Corneal edema
   - Fonn et al and others
5. ↓ Limbal injection
   - Papas and others
6. ↓ Myopic shift
   - Dumbleton et al
7. ↓ Endothelial polymegathism
   - Fonn et al

Absence of chronic tissue changes WITH IMPROVED OXYGEN PERFORMANCE

What about Daily Disposables Effect on CIEs

- **Radford 2009**
  - Overall increased risk of CIE for DD
    - Attributed to one lens type
- **Chalmers OVS 2010 and IOVS 2011**
  - Daily disposables had no effect in CIE risk
    - They did not reduce the risk either!
- **Chalmers OVS 2012**
  - 4X protective effect for CIE across modes of wear
  - 12X protective effect for CIE during DW only
What about SH and solution hypersensitivity?

Is it on the rise?
- Are certain solutions/lenses associated?
- What good studies are there?
  - Chalmers et al OVS 2012

### Analysis of Events with Multiple Infiltrates per Eye

<table>
<thead>
<tr>
<th>Factors</th>
<th>Univariate Odds Ratio</th>
<th>Multivariate Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>p-value</td>
<td>p-value</td>
</tr>
<tr>
<td></td>
<td>(Ref)</td>
<td>(Ref)</td>
</tr>
<tr>
<td>Number of Infiltrates</td>
<td>81 (59, 88)</td>
<td>124 (75, 100)</td>
</tr>
<tr>
<td>Silicone Hydrogel (hydrogel)</td>
<td>3.68 (1.51, 8.70)</td>
<td>3.42 (1.57, 7.47)</td>
</tr>
<tr>
<td>Extended Wear (Daily Wear)</td>
<td>2.18 (1.07, 4.43)</td>
<td>2.18 (1.07, 4.43)</td>
</tr>
<tr>
<td>Age (Per Yr Older)</td>
<td>0.81 (0.80, 0.83)</td>
<td>0.81 (0.80, 0.83)</td>
</tr>
</tbody>
</table>

**Significant Multivariate Risk Factors**

<table>
<thead>
<tr>
<th>Factors</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds Ratio</td>
<td>Odds Ratio</td>
</tr>
<tr>
<td></td>
<td>(Ref)</td>
<td>(Ref)</td>
</tr>
<tr>
<td>Reusable BCL (Daily Wear)</td>
<td>4.13 (1.71, 9.83)</td>
<td>2.14 (1.54, 10.62)</td>
</tr>
<tr>
<td>Extended Wear (Daily Wear)</td>
<td>3.98 (2.33, 6.44)</td>
<td>N/A</td>
</tr>
<tr>
<td>Silicone Hydrogel (hydrogel)</td>
<td>1.72 (0.97, 3.05)</td>
<td>1.99 (1.06, 3.75)</td>
</tr>
<tr>
<td>Age (Per Yr Older)</td>
<td>0.95 (0.64, 0.98)</td>
<td>0.95 (0.63, 0.97)</td>
</tr>
</tbody>
</table>

81 multiple CIEs include: 2 MK, 2 CLPU, 45 IK, 9 CLARE, 13 solution hypersensitivity, 3 viral, 7 ARK
The Longitudinal Analysis of Silicone Hydrogel (LASH) Contact Lens Study

- 205 patients in lotrafilcon A 30 day CW
- Primary outcome: CIE
- Main exposure: Corneal staining
- Other key/interacting variable: Bacterial contamination of study lenses, Indirect assessment of mucin layer/mucin balls

CONCEPTUAL MODEL FOR CIE

Microbial contamination → CIE

Presence of Ocular surface Disruption (staining or disrupted mucins)
Exam Times & Procedures

SLIT LAMP EXAM, STAINING & CIE CULTURES

0 1 4 8 12

Unadjusted cumulative probability of remaining CIE free in the LASH Study over 1 year of follow-up

38 subjects experienced at least one CIE
KM unadjusted cumulative incidence of survival = 73.3% (95% CI 65.0%-79.9%)
KM unadjusted cumulative incidence of CIE = 26.7% (95% CI 20.1%-35.0%)

Unadjusted cumulative probability of remaining CIE free stratified by presence or absence of substantial bioburden on study lenses

Univariate Hazard Ratio through 12 months
4.41 (95% CI 2.21-8.79)
### Percentage of subjects with culture positive lenses stratified by visit and presence of infiltrate

<table>
<thead>
<tr>
<th></th>
<th>No Infiltrative Event</th>
<th>During Infiltrative Event</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any event</td>
<td>Asymptomatic Events</td>
</tr>
<tr>
<td>Substantial bacterial bioburden</td>
<td>14%</td>
<td>65%</td>
</tr>
</tbody>
</table>

*p value compared to asymptomatic events

### Substantial lens bioburden is associated with at least an 8 fold (800%) increased hazard for a CIE regardless if the CIE is symptomatic or not

### Unadjusted cumulative probability of remaining CIE free stratified by presence or absence of at least one episode of moderate corneal staining or greater

![Graph showing unadjusted cumulative probability of remaining CIE free stratified by presence or absence of at least one episode of moderate corneal staining or greater]
**Mucin Ball Depressions**

<table>
<thead>
<tr>
<th>Surface Area</th>
<th>Density</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. 1 - 15%</td>
<td>1. Very Slight</td>
</tr>
<tr>
<td>2. 16-30%</td>
<td>2. Slight</td>
</tr>
<tr>
<td>3. 31-45%</td>
<td>3. Moderate</td>
</tr>
<tr>
<td>4. &gt;45%</td>
<td>4. Severe</td>
</tr>
</tbody>
</table>

**Unadjusted cumulative probability of remaining CIE free stratified by presence or absence of repeated episodes of mucin ball formation**

Univariate Hazard Ratio

0.17 (95% CI 0.06-0.43)

**Mucins in healthy tears**

- At least 4 of 19 mucin genes found on the ocular surface
  - Soluble MUC5AC secreted by goblet cells for viscosity
  - Membrane spanning mucins: MUC1 and MUC16 secreted by corneal and conjunctival epithelium
  - MUC4 secreted by conjunctival epithelium

May represent a different mucin profile which renders a subject less likely to conjugate the immune response against bacterial ligands
Risk Factor Analysis for CIE

- Corneal Staining: Not associated with bacterial contamination
- Bacterial Contamination: 800% increased risk
- Smoking: 400% increased risk
- Alcgin Balls: 84% decreased risk

What is the rate of Lens, Case and Care System Contamination?

- Lenses: >50% harbor micro-organisms; 10% pathogenic
- Care Systems: All can be contaminated, including up to 30% of preserved products
- Cases: >50% contamination

LASH Study: Lens Microbiology
Pathogical organisms found at least one visit

- Yes: 68%
- No: 32%

(From Microbial Contamination of Contact Lenses and their Accessories: A Literature Review. Szczotka-Flynn, Pearlman, Ghannoum. ECL, March 2010)
**Lens Organisms: Frequency (%) of isolation in LASH Study**

- Lenses: Frequency (%) of isolation across all visits

**Lens Contamination**

- The presence of ocular pathogens is typically sporadic and unpredictable.
- Variable opinions on whether silicone hydrogel lenses differ from traditional pHEMA lenses in terms of levels or frequency of bacterial colonization in vivo.
- Lens handling greatly increases the incidence of lens contamination.
- The ocular surface has a tremendous ability to destroy organisms.

**Hand Washing and Contact Lens Contamination**

- Little effect is achieved on the reduction of resident flora with typical hand washing procedures. Therefore, infections or inflammation contact lens complications related to resistant hand flora are still probable, even in patients who comply with these procedures.
The Ocular Immune Response

- Two types of immune response:
  - Innate
    - First line of defense
    - Rapid onset (minutes)
    - Lacks memory
    - Lacks more aggressive response following subsequent exposure
  - Adaptive
    - Humoral (antibody) and cell-mediated pathways
    - Longer time frame (hours or days)
    - Three phases:
      - Antigen recognition and presentation to host T cells
      - Antigen processing and activation of T and B cells and effector lymphocytes
      - Mature cells interact with target antigen
    - Memory! Subsequent exposure generates a more aggressive response.

The Innate Response

- In the eyes: bony orbit, blink reflex, tear film with anti-inflammatory and anti-microbial proteins, commensal bacteria, tight junctions of corneal epithelium, B-defensins, alternate pathway of complement, pattern recognition receptors

If microbes are present at the site of an inflammatory response, how are they recognized as “foreign”? 
Innate immunity: activation

- Some components of innate host responses are constitutive and fully or partially active at all times:
  - Barrier functions of skin and mucous membranes (mechanical)
  - Lysozymes, proteolytic enzymes, acid, etc which exist in tears, and other body fluids such as in the stomach (chemical)
- Other innate defense mechanisms require short term activation........

How can bacterial initiate the immune response?

- We live in a virtual sea of bacteria with which we peacefully co-exist........most of the time.
- Bacteria can cause disease by:
  - "invading" a space where they are not "normally" found
  - Producing toxins
  - Immunopathology– sometimes the immune response is the disease

Toll Like Receptors (TLR’s) are A Class of PRR’s

- Signaling through various combinations of TLR’s activates the epithelial cells to produce inflammatory cytokines and chemokines
- The cytokines/chemokines recruit white blood cells (mostly PMNs) to the site of insult so they can phagocytose and kill the microbe
<table>
<thead>
<tr>
<th>TLR2 + TLR6</th>
<th>Bacterial components: Peptidoglycan, Zymosan (Yeast), GPI anchor of T. cruzi, Lipoarabinomannan and phosphotidylinositol dimannoside (MTB)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLR3</td>
<td>Double stranded (viral) RNA</td>
</tr>
<tr>
<td>TLR4</td>
<td>LPS, Taxol, HSP60, fibronectin extra domain A, respiratory syncytial virus F protein</td>
</tr>
<tr>
<td>TLR5</td>
<td>Bacterial Lipoproteins</td>
</tr>
<tr>
<td>TLR9</td>
<td>Hypo-methylated CpG</td>
</tr>
</tbody>
</table>

Underhill & Ozinsky, Current Opinion Immunol, 14: 103-110, 2002

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Bacterial plasma membranes are surrounded by a cell wall composed of a repeating polymer of peptides and sugars (peptidoglycan). The cell wall is relatively thin in Gram negative bacteria and thicker in Gram positive bacteria.

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Several bacterial components such as Peptidoglycan, LPS, and bacterial DNA serve as TLR ligands which can initiate innate inflammatory responses.

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Underhill & Ozinsky, Current Opinion Immunol, 14: 103-110, 2002
Mouse model of Contact lens associated corneal inflammation

- Epithelial abrasion
- 2 µL LPS or other microbial product added to corneal surface
  - From diameter punch from contact lens placed on ocular surface 2h
  - Or soak CL in LPS
- Lens removed, mice wake up
- Measure CXC chemokines at 6 hours
- Dissect and ELISA
- Neutrophil infiltration to corneal stroma, corneal thickness and haze at 24 hours
  - Confocal microscopy to measure infiltrate
  - Immunohistochemistry for neutrophils
**Central corneal stroma 24h after topical exposure to LPS**

Normal C57Bl/6  
LPS treated C57Bl/6

Infiltrates evident, highly refractile cells

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**Treatment**

- Antibiotics
- Steroids
- Removal of antigen/removal of CL

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**Prevention, Prevention, Prevention**

*Cartoon Image: The Doctor Specializes in Prevention Medicine. So if you’re already sick, he’s not interested.*

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**Figure 1-10** Prevention and therapy aimed at initially vectorial activities. (From Wilson T, Ziggie’s cartoon, Universal Press Syndicate, 1991)
Prevention

- Lid Hygiene?
- Antibacterial coated lenses?
- Antibacterial coated cases?

Antimicrobial Cases

- Decreased microbial contamination of lenses stored in silver ion case

Elafilon A Lens Recovery Plates. Clockwise from Top Left: AQuify MPS-Soaked Lenses in PRO GUARD Silver Case, ReNu with Moisture Loc-Soaked Lenses in ReNu Case, Opti-Free Express-Soaked Lenses in Opti-Free Case, AQuify MPS-Soaked Lenses in Standard AQuify MPS Case.

Thank you