Prescribing Contact Lens Solutions: Making Informed Decisions

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Financial Disclosure
William D. Townsend, O.D., F.A.A.O.

• William D. Townsend OD has received honorarium from Alcon, Allergan, CIBA, Cooper Vision, Odyssey Medical, and VSP. He is not on the board of any ophthalmic drug or contact company

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Why do patients drop out of CL’s?

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<th>RGP</th>
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<td>40%</td>
<td>58%</td>
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<tr>
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When patients present with contact lens-associated discomfort......

• Change the fit
• Change the material (wetter)
• Change the brand
• Add re-wetting drops
• Try punctal plugs
• Evaluate for solution-related complications, compatibility

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• As a paid speaker I have been sponsored by several companies including Alcon, Allergan, CIBA, Cooper Vision, Odyssey Medical, and VSP
• I am not a consultant to nor an employee of any pharmaceutical or industry company.
• Any product superiority mentioned during this presentation will be supported by scientific studies and white papers

2010-Contact Lens Dynamics in US Market

Sources: Nielsen Household Panel, IPSOS NPD Tracker Consumer Surveys, Alcon estimates

Blissful

Dissatisfied (Tolerant Sufferer)

New wearers
3.0 million/year

Base of 30.2 million soft CL wearers (54% > 35 yrs old)

Lost to CL wear
3.0 million (10%) per year

1.0 M undergo refractive procedures 800 K

Post-Refractive Lens Wear 10% of Procedures 80 K

Borderline SCL wearers

WHY?

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Why patients drop out

- Vision
  - Presbyopia inadequately corrected
  - Dryness
- Poor lens surface quality
- Convenience—should not be an issue
- Comfort #1
  - Poor fit
  - Dryness (actual or perceived)
  - Loss of surface conditioning
  - Coated lens surfaces
  - Solution allergy
  - Solution toxicity
  - Solution-related

Our goal today is...........

- Identify solutions problems unique to hydrogel lens “groups”
- Identify solutions problems unique to silicone hydrogel lenses
- Review known adverse interactions between lens materials and solutions
- Empower you with a scheme for evaluating future CL solutions and drops
- Lower the rate of CL dropouts your practice

Milestones in CL Solutions, Materials

- Soft lenses introduced - 1971 Bausch & Lomb
- Heat disinfection - 1971
- Thimerosal - 1977 Flexsol & Flexcare BP/Alcon
  - High rate of allergy
- Chlorhexidine - SoftMate Disinfecting Solution BH
- New generation solutions - 1980’s lower toxicity
- Old solutions not necessarily compatible with new materials
- New solutions may not be compatible with old materials

Crucial Issues in Choosing CL Solutions - What Patients Want

- Comfort
- Convenience
- Cost
- Confidence
- Compliance
  - What did the doctor or tech tell them?

Crucial Issues in Prescribing CL Solutions - What Doctors Want

- Eye-Solution compatibility
- Lens-Solution compatibility
- Lens-Surface wettability
- HAPPY PATIENTS who continue to wear contacts and support your practice

2010: Great expectations from multipurpose contact lens solutions?

- Kill bacteria, viruses, fungi, amoeba
- No rubbing required
- Compatibility with tear pH, osmolarity
- Compatibility with all CL materials
- Stability over life of the container
- Wet and condition the lens surface
- Enhance comfort of CL wear
- Affordability
Improving Lens Comfort
Are There Differences Between MPS Products?

COMFORT Influenced by: Wettability + Cleanliness + Compatibility

- Lasting surface wettability
- Absence of pathogens, debris and protein
- Dynamic wettability test over time
- Disinfection testing
- Lysozyme removal
- Minimize ocular stress
- Corneal staining

Factors that influence informed solution prescribing decisions

- Lens material: water content, ionic vs non-ionic, silicone hydrogel vs hydrogel
- Use: daily vs. extended vs. flexible wear
- Protein coating/uptake characteristics
  - Hydrogel vs. silicone hydrogel
  - Location, depth, and denaturing
- Patient history
  - Infection, keratitis
  - Allergy
  - GPC
  - Other
- Physical exam

Making informed decisions: we do it all the time!

- 48 yo male with large internal hordeolum
- HIV positive with T-cell count of 120
- No prescription drug coverage w/ insurance

What is your decision making process?

- I need a bactericidal drug.
- I need a drug w/ good gram+ coverage.
- I need a drug w/low incidence of resistance.
- I need a generic drug to keep cost down.

Your solution is to prescribe........ Augmentin 875 mg Q 12 hours!

But how do we make informed decisions in prescribing CL solutions?

- Hydranate
- Potassium chloride
- Methylcellulose
- Polyquad
- Group 2 Lenses
- Tetronic 1304
- PHMB
- Citrate
- Pluronic
- Edetate disodium
- Sodium borate
- Povidone
- Tetronic 1107
- Dymed
- Poloxamine
- Alexidine

Hydrogel Lens Groups

- Created in 1986 for solution companies
- Categorized “for purposes of evaluating effects of accessory products on the lens materials”
- Based on water content and ionic charge
- “Low water“- less than 50 % water content
- “Low water“- all others
- “High water“- (highly charged) materials
- “Non-ionic“- (low charge) surfaces
Contact Lens Materials Groups

<table>
<thead>
<tr>
<th>GROUP 1</th>
<th>GROUP 2</th>
<th>GROUP 3</th>
<th>GROUP 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Water (&lt;50% H₂O)</td>
<td>High Water (&gt;50% H₂O)</td>
<td>Low Water (&lt;50% H₂O)</td>
<td>High Water (&gt;50% H₂O)</td>
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<tr>
<td>Non-ionic Polymers</td>
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<td>Ionic Polymers</td>
<td>Ionic Polymers</td>
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<td>Cibasoft Preference CSI</td>
<td>Gold Medalist Toric Soflens 66 Proclear</td>
<td>Acuvue sphere</td>
<td>Acuvue monthly Focus Toric</td>
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<td>Soflens</td>
<td>Focus Dailies</td>
<td>Biomedics Toric Biomedics 55</td>
<td></td>
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</table>


Fig. 9 - The quantity of the protein deposited on lens channel with different care solutions.
Material does make a difference!

Hydrogel vs. Silicone Hydrogel Lens

- **O₂ Permeability**
  - Increased H₂O content HG = increased O₂
  - Increased H₂O content SiHG = decreased O₂

- **Lipid coating**
  - Rare in hydrogels
  - Very common in silicone hydrogels - must rub!

- **Protein coating**
  - Hydrogels - minimal denaturing
  - Silicone hydrogels - extensive denaturing

- **Matrix absorption of preservative a factor?**
  - Hydrogel - yes
  - Silicone hydrogel - no

What goes into a CL solution?

- Water (actually, really good water)
- Electrolytes
- Cushioning agents
- Chelating agents
- Preservatives / Disinfectant
- Buffering agents
- Cleaning agents
- Wetting / Conditioning agents

Early Preservatives

- **Thimerosal**
  - Mercurial compounds
  - Allergies
- **Benzalkonium Chloride (BAK)**
  - Cationic detergent
  - Affects lens wettability & tear film stability
  - Concentrates in lens matrix, released later
  - Causes toxic keratitis
- **Chlorhexidine**
  - Biguanide germicidal agent
  - Less sensitization than thimerosal, but toxic to epithelium
- **Sorbic Acid** - discolors lenses

21st Century Preservatives

- **Aldox** (methylidipropyldimethylamine) Small MW = 300
  - Anti-fungal activity
  - Acanthamoebicidal activity
  - Anti-bacterial activity
- **Alexidine** Small MW = 500
  - Biguanide used in dentistry since mid '70's
  - Causes cell lysis by interference with the layer phospholipid of the microorganism's cytoplasmic membrane
- **Polyhexamethylene biguanide (PHMB)** Medium MW = 800
  - Biguanide class (includes chlorhexidine)
  - Anti-microbial efficacy
  - Cytotoxic reactions dependent on concentration
- **Polyquad** (polyquaternium-1) Large MW = 8,000
  - Reduced cytotoxicity
  - Potent bactericide
  - Large molecule reduces absorption
Why patients (and doctors) are confused

- FDA “stand alone criteria”
  - After inoculation, solution must show:
    - Three log units of kill for bacteria
    - One log unit of kill for fungi
- MPS (not stand alone)- cleans, disinfects, rinses, and stores
  - (rubbing required)
- MPDS (stand alone)- same as MPS but higher disinfectant criteria
  - (no rubbing required)

Potential Preservative-Lens-Eye Interactions

- Preservatives may:
  - Adsorb (attract and hold to surface minute particles of mixture or molecules of gas or liquid)
  - Absorb (to take something in through pores on surface and into lens matrix)
  - Be released onto the ocular tissue possibly resulting in a potential cytotoxic response
  - These may occur more frequently with small molecule preservatives
- Prevention of above requires blockage of lens sites to prevent adsorption and release

Strategies to Reduce Ocular Exposure to Cytotoxic Substances

- Use a large MW preservative or molecule with minimal ionization
- Prevent lens adsorption or release of offending chemical
- Provide shielding of lens using a charged molecule (ie. citrate)
- Modify preservative size & charge to reduce adsorption and release

OPTI-FREE EXPRESS MPDS vs. ReNu Multi-Plus Staining

Opti-Free Express VS ReNu Multi-Plus

OPTI-FREE EXPRESS MPDS vs. ReNu Multi-Plus

Comfort

P = 0.04

P = 0.04


OPTI-FREE EXPRESS MPDS vs. Complete MPS

Staining

Lessons to be Learned

• Staining occurs with all preservatives selectively worse in 1st 6 hours of wear
• Polyquad preserved solutions show less staining at 2-4 hours compared to PHMB-preserved solutions
• PHMB staining is proportional to concentration if all other components in solution are the same
  ➢ But they are not!
  ➢ Differences in staining not explained by preservative alone

Preservatives and Anti-microbial Activity?

• Must kill pathogens, especially gram negative (pseudomonas)
• Must kill amoebae
• Must act within hours
• Must have low toxicity to ocular tissue


Dannelly H and Waworuntu R. Effectiveness of Contact lens disinfectants after lens storage. Eye and Contact lens, March 2004
Buffering Agents in CL Solutions

- **Stable lens parameters**
  - Acidic pH promotes lens dehydration and steepening (tighter fit of the lens on the cornea);
  - Alkaline pH promotes hydration and flattening (looser fit on the cornea).

- **Tear pH affects cleaning efficacy of surfactants**

**Buffering Agents in CL Solutions**

- As washing proceeds, the alkalinity or pH drops
- Under acidic (low pH) conditions, cleaning is reduced.
- Buffering agents
  - Stabilize the pH and lens shape
  - Enhance the cleaning attributes of the solution
  - May positively or negatively affect toxicity of disinfectants on the eye

Buffers and Lysozyme Removal

- 90% of tear protein is lysozyme
- Borate-buffered solutions marginally remove lysozyme
- Citrate-buffered solutions maximally remove lysozyme
  - Citrate molecule is negatively charged and pulls protein away from lens surface

**Cleaning & Wetting Agents**

- Important for removal of surface contaminants
- Can positively or negatively affect surface wettability
- Can be customized to increase lipophilicity and hydrophilicity

**FDA Guidelines**

- Recent recalls suggest that present standards, methods not realistic, effective
- Need more “real-life” strategies for evaluating contact lens solutions, drops

Log Reduction after 8 hours

Dannely H and Waworuntu R. Effectiveness of Contact lens disinfectants after lens storage. *Eye and Contact lens*, March 2004
Proteins in the Eye

- Every protein in our body has a function.
  - **Lysozyme**: The main protein found in tears; primarily has antimicrobial activity
- Proteins can be found in two states
  - **Native State**: natural (folded) state
  - **Denatured State**: forms deposits which bind to the surface of the lens and cause irritation
    - Can be recognized by immune system as "non-self"
    - Can lead to development of GPC
- Cleaner/conditioner can prevent binding of denatured proteins to hydrogel or silicone hydrogel lenses

**Tetronic Structure**
- ethylene oxide (hydrophilic)
- propylene oxide (lipophilic)
- bridge molecule (diamine)

**Pluronic Structure**

Tetronic Block Copolymers

The Tetronic® surfactants are tetra-functional block copolymers based on ethylene oxide and propylene oxide. They function as anti-foaming agents, wetting agents, dispersants, thickeners, and emulsifiers. (BASF literature)

EW Lysozyme Deposit Curve

Acuvue 2 w/ no Solutions

Inter-Patient Variability

Patients coat lenses differently!

O FX vs ReNu Multiplus

(3 Crossover studies combined)

AV-2 DW (after Rub/Rinse & overnight soak)
Hydrogel Considerations
• Hydrogel lenses, particularly high-water types, attract protein
• Mucin and lipid deposits are a little less problematic in hydrogels
• Select a solution that minimizes hydrogel coating with protein
• Select a lens material that has reduced dehydration attributes
  ➢ Proclear 62% water
  ➢ Extreme H2O 59% water

Where are we headed with lens materials and solutions?
• Silicone hydrogels gaining in market share
• Increasing use as daily wear
• New materials designed for compatibility with these lenses
• Matched lenses materials by labels
  ➢ B&L- Pure Vision with Renu MoistureLoc
  ➢ B&L- Biotrue and Purevision
  ➢ CIBA- Night & Day with AQuify

What about new solutions, old materials?
• 30 patients in 3 diverse geographic locations
• Compared OFX to ReNu MoistureLoc for staining, comfort and wearing time
• Non-masked study, crossover using Accuvue 2 lenses
• Evaluated at entry, 2 weeks, and exit

Crucial Issues in Compatibility
• Which lens material and solutions are compatible?
• Which lens material and solutions are not compatible?
• Is there a source for answering the above questions?

Townsend, Katims, & Rosen. Investigating a New-Generation Multi-Purpose Solution Contact Lens Spectrum December 05
• Mean staining grade for ReNu MoistureLoc was 0.97 compared with 0.52 for Opti-Free Express.
• Mean staining area was 1.6 for all segments for ReNu MoistureLoc while mean staining area was 1.2 for all segments for Opti-Free Express
• Optifree Express was preferred by a greater number of participants in several categories including overall comfort, keeping lenses comfortable for longer, ease of handling, better vision, and reduced sensation of dryness.

<table>
<thead>
<tr>
<th>Lens and Solution Combinations</th>
<th>Accuvue 2*</th>
<th>PureVision*</th>
<th>ReNu MoistureLoc</th>
<th>ReNu MultiPlus</th>
<th>Wal-Mart Equate*</th>
<th>Complete MoisturePlus</th>
<th>Acuvity*</th>
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<td>Unisol 4® Off-Label</td>
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<td>2%</td>
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Andrasko Corneal Staining Grid
Lens and Solution Combinations

Polyquads & Biguanides
The "Conditioning Concept"

- Lenses out of the blister pack have certain features that are lost after wear.
- Maintaining that "conditioned" surface probably helps patient comfort; therefore retention.

What Really Happens?

- Bulk water loss from a hydrophilic lens is minimal regardless of intrinsic water content or lens group.
- Drying occurs on the lens surface, but is much more than water loss!
- Changes in lens surface wetting can be measured by wetting angle measurement.
- Surface drying may be related to decreased lubricity and discomfort (Lid Wiper Epitheliopathy).

Hydrophilic versus Hydrophobic Molecular Orientation at the Contact Lens Surface

AQuify?

- Formulated for use with Ciba’s Focus Night & Day lenses.
- Unique formulation allows overnight or 5-minute disinfection (RUB).
- Buffering agents may have advantages over other solutions.
- High wetting angle when used with hydrogels and silicone hydrogels.
- Good staining profile.

AQuify

- Good choice for most silicone hydrogels—especially Night & Day.
- HydroLock® lubricating system:
  - Dexamethasone (ProVitamin B5), a moisturizer.
  - Sorbitol, a humectant.
- Unique time option:
  - 5 minute soak with rub.
  - 4 hour soak without rub.
- Effectively removes lipid, the "culprit" in silicone hydrogels.

Amos C. Performance of a New Multipurpose Solution Used with Silicone Hydrogels.

- Compared staining in Night & Day patients using ReNu MultiPlus and AQuify MPS.
- Both preserved with PHMB 0.0001%.
- After one month:
  - ReNu group-24% showed staining.
  - AQuify group- no staining.
- Why? Concentration of PHMB same.
- Formulation is the difference.
Optifree RepleniSH
• Specifically formulated for SiHy compatibility (also hydrogels)
• Excellent wetting angles with hydrogel and SiHy
• Some issues with hypersensitivity not seen in original Optifree Express

CIBA Vision- Clear Care
• One bottle peroxide-based solution
• Bubbling action removes surface contaminants
• Contains Pluronic 17R4 as a cleaning agent
• No conditioning agent!
• Very high wetting angles

Amos: Waterloo Study
• Compared Clear Care with Opti-Free Express patients wearing Night & Day daily wear
• After 1 month
  ➢ 0% of Clear Care had staining
  ➢ 8% of Opti-free had staining

My opinion...
• Hydrogen peroxide systems are safe, easy to use and have virtually no toxicity issues unless put into eye
• One-step systems not effective in killing Acanthamoeba cysts because of rapid neutralization
• Lack any conditioning agent
  ➢ Very high wetting angle
  ➢ Great for people with solution allergy

FDA Guidelines
• Recent recalls suggest that present standards, methods not realistic, effective
  ➢ Ciba Aquify recalled November 2005
  ➢ B&L MoistureLoc recalled April 2006
  ➢ AMO Complete recalled May 2007
• All used biguanide-based preservatives
• Need more “real-life” strategies for evaluating contact lens solutions

AMO Complete Recall: The Facts
• 46 patients developed (AK) since January 2005
• 39 of these patients wore soft contact lens
• 21 of the CL wearers reported using Complete
• CDC estimates at least seven times greater risk of AK for those who used Complete
AMO Complete - What happened?

- Acanthamoeba
  - Shape oval to triangular when moving
  - Eukaryote - like us
  - Form cysts when stressed
  - Needs break to enter cornea
  - EPA water standards have changed
    - Water supplies w/ amoebae now OK for consumption

The Future

- Better lens surfaces
- Better understanding of lens surface - solution interaction
- Better ways to prevent & remove deposits
- Better ways to condition lens surfaces
- Better molecules to kill pathogens

New Solutions

- Dual disinfection the new standard
- RevitaEyes
  - Preserved with polyquaternarium and alexidine
- BioTrue
  - Preserved with polyquaternarium and PHMB
  - Addition of hyaluronan

Prescribing Solutions

- Prescribe, Prescribe, Prescribe
- Evaluate lens material characteristics
- Know potential interactions between solutions, materials
- Understand that patients will change solutions unless you educate them!

Conclusion

- No solution works for every patient every time!
- Follow the literature as studies are published
- Be critical of the intent of the authors
- Use lid eversion and fluorescein staining to accurately evaluate your contact lens patients compatibility with solutions
- Always consider solution-related complications or interactions when you are problem solving comfort issues