Prescribing Contact Lens Solutions: Making Informed Decisions

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2010-Contact Lens Dynamics in US Market

Why do patients drop out of CL’s?

<table>
<thead>
<tr>
<th>Reason</th>
<th>Soft</th>
<th>RGP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discomfort</td>
<td>40%</td>
<td>58%</td>
</tr>
<tr>
<td>Dry eye symptoms</td>
<td>10%</td>
<td>11%</td>
</tr>
<tr>
<td>Red eye symptoms</td>
<td>5%</td>
<td>3%</td>
</tr>
<tr>
<td>Insertion/removal</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Poor vision</td>
<td>5%</td>
<td>7%</td>
</tr>
<tr>
<td>Advised by doctor</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Other (cost, presbyopia, photophobia, no answer)</td>
<td>23%</td>
<td>11%</td>
</tr>
</tbody>
</table>

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

Disclaimer
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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.
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

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?

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

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
Improving Lens Comfort

Are There Differences Between MPS Products?

COMFORT Influenced by: Wettability + Cleanliness + Compatibility

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

<table>
<thead>
<tr>
<th>Hydrogel Lens Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Created in 1986 for solution companies</td>
</tr>
<tr>
<td>Categorized “for purposes of evaluating effects of accessory products on the lens materials”</td>
</tr>
<tr>
<td>Based on water content and ionic charge</td>
</tr>
<tr>
<td>“Low water”- less than 50 % water content</td>
</tr>
<tr>
<td>“High water”- all others</td>
</tr>
<tr>
<td>“Ionic”- (highly charged) materials</td>
</tr>
<tr>
<td>“Non-ionic”- (low charge) surfaces</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group 2 Lenses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydranate</td>
</tr>
<tr>
<td>Potassium chloride</td>
</tr>
<tr>
<td>Polyquad</td>
</tr>
<tr>
<td>Group 2 Lenses</td>
</tr>
<tr>
<td>Tetronic 1304</td>
</tr>
<tr>
<td>Citrate</td>
</tr>
<tr>
<td>Edetate disodium</td>
</tr>
<tr>
<td>Povidone</td>
</tr>
<tr>
<td>Tetronic 1107</td>
</tr>
<tr>
<td>Dymed</td>
</tr>
<tr>
<td>Poloxamine</td>
</tr>
<tr>
<td>Alexidine</td>
</tr>
</tbody>
</table>
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>
</tr>
<tr>
<td>Non-ionic Polymers</td>
<td>Non-ionic Polymers</td>
<td>Ionic Polymers</td>
<td>Ionic Polymers</td>
</tr>
<tr>
<td>Cibavision Preference</td>
<td>Gold Medalist Toric</td>
<td>Soflens 66 Proclear</td>
<td>Hydrocurve II 45</td>
</tr>
<tr>
<td>Softens</td>
<td>Soft Mate B</td>
<td>Durassoft 2</td>
<td>Acuvue sphere</td>
</tr>
<tr>
<td>Focus Dailies</td>
<td>Focus monthly</td>
<td>Focus Toric</td>
<td>Acuvue Advance</td>
</tr>
<tr>
<td>Focus Night/ Day</td>
<td>PureVision</td>
<td>Biomedics Toric</td>
<td>PureVision</td>
</tr>
<tr>
<td>Silicone hydrogels</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


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** (myristamidopropyl dimethylamine) 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 absorption and release


- Two randomized, investigator-masked, 2-month crossover studies
- Study 1- 45 subjects used Opti-Free Express & Complete for 1 month then crossover
- Study 2- 44 subjects used Opti-Free Express and ReNu MultiPlus for 1 month then crossover
- Lenses used:
  - Accuvue 2- group 4
  - Soflens 66- group 2

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
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

Log Reduction after 8 hours
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

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

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

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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 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!

**OFX 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?
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

Amos C. Performance of a New Multipurpose Solution Used with Silicone Hydrogels. Optician 2004

- 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

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
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
- RevitalEyes
  - 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