Giant papillary conjunctivitis (GPC) and allergic disease

presented by
Louis J. Catania, O.D., F.A.A.O.
for
The Vision Institute of Canada Conference
Saturday, November 8, 2008
5:00 to 5:30

Clinical Immunology

Type I: Cell Mediated Response
“Delayed hypersensitivity reaction”

Type IV: Immediate IgE Response

Clinical Immunology

Acute inflammation
- Vasodilation
- Edema
- Infiltration
- Ulceration

Subacute/Chronic
- Edema
- Granuloma
- Granulation
- Induration
- Caseation
- Neovascularization/Pannus
- Repair/Healing/Scarring
  (Corneal Remodeling)
- Loss of tissue function
White blood cells (WBCs) *Leukocytes*

<table>
<thead>
<tr>
<th>Monocytes</th>
<th>Polymorphonuclear Cells (PMNs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macrophage</td>
<td>• Neutrophil</td>
</tr>
<tr>
<td>Monocyte</td>
<td>• Basophil</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>• Eosinophil</td>
</tr>
</tbody>
</table>

Normal condition:

- 70% avascular (in tissue)
- 30% vascular (in blood)

Normal condition:

- 100% vascular (in blood)

Mast Cells

- 50 million mast cells are present in the human eye
- In quiet eye, most are in substantia propria
- In an allergic state, they are found in more superficial layers.
- Eye rubbing degranulates mast cells (Greiner 1985)
- 2 different mast cell subtypes exist in different tissues (called heterogeneity)
  - Tryptase (*T*) type small intestines and lungs
  - Tryptase/Chymase (*TC*) type in skin and eye
- *TC* mast cells have 60X more histamine than *T* type

Antigen Presenting Complex

Antigen $ightarrow$ Antigen Presenting Cell eg. Macrophage 

$\rightarrow$ HLA Receptors

$\rightarrow$ T Cell

$\rightarrow$ Activated T Cell

$\rightarrow$ APC

Mast Cells

- Antigen taken up, processed and bound to surface of Antigen Processing Cell APCs
- Allergen/APC complex activates Th2 lymphocyte which in turn activates Naïve B cells to proliferate and differentiate
- Plasma cell secretes allergen specific IgE which binds to sensitized Mast Cells
- Mast cell degranulates releasing cytokines
- Chemical mediators recruit and activate leukocytes
### The Allergic Cascade

Moving downstream towards disaster!

<table>
<thead>
<tr>
<th>Clinical Sequence</th>
<th>Duration</th>
<th>Immunologic Sequence</th>
<th>Pharmacologic Sequence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Sequence</td>
<td>Days to weeks</td>
<td>Immunologic Sequence</td>
<td>Pharmacologic Sequence</td>
</tr>
<tr>
<td>* Hx of allergies</td>
<td></td>
<td>IgE mediated response</td>
<td>Cold compresses</td>
</tr>
<tr>
<td>* Seasonal allergies</td>
<td></td>
<td>Mast cell degranulation</td>
<td>Pharyngeal MCS</td>
</tr>
<tr>
<td>* Asthma</td>
<td></td>
<td>Early phase degranulation</td>
<td>Antihistamines</td>
</tr>
<tr>
<td>* Minimal ocular symptoms</td>
<td></td>
<td>Mild histamine release</td>
<td>Patient education &amp; counseling</td>
</tr>
<tr>
<td>* Rhinitis</td>
<td></td>
<td>Degranulation</td>
<td>Antihistamines</td>
</tr>
<tr>
<td>* Minimal ocular symptoms</td>
<td></td>
<td>Histamine release</td>
<td>Particularly H1</td>
</tr>
<tr>
<td>* Quality of life compromised</td>
<td></td>
<td>Symptomatic &amp; cytokines</td>
<td>Antihistamines</td>
</tr>
<tr>
<td>* Acute/subacute reactions</td>
<td></td>
<td>Prostaglandin activity</td>
<td>Prophylactic MCS</td>
</tr>
</tbody>
</table>
| * Increasing subjective symptoms | | Vasodilation | Anesthetic (?)
| * Increasing physical signs | | Edema (plasma leakage) | Anti-eosinophilics (neodocr.) |
| * Quality of life impaired | | Cell mediated response | NSAIDs (if) |
| * Quality of life impaired | | Tissue destruction | Steroids |
| * Acute/subacute reactions | | Risk of ulcerations | Oral antihist/decongestants |
| * Quality of life impaired | | Disabling to patient | Steroids (Topicals and orals) |
| * Acute/subacute reactions | | | Immunotherapies |
| * Quality of life impaired | | | Tissue rehabilitation |

#### Thank you

lcatania@bellsouth.net
Subjective...

- "Sandy, gritty feeling"
- Foreign body sensation
- Nonspecific ocular surface" dryness," discomfort, or burning irritation
- Dust
- Smoke (eg, especially cigarettes, cigars)
- Fumes (and pollution)
- Fine particles (eg, fabrics, threads, spores)
- Air-conditioning (with dehumidification) and home heating systems

Subjective...

- Antihistamines (especially nonprescription chlorpheniramine)
- Decongestants
- Diuretics
- Atropine-based compounds
- Oral steroids
- Birth control pills (uncertain)
- Alcohol-based medications (or plain old "booze")

Dermatological conditions

- Seborrhea
- Variable dermatites
- Eczema
- Psoriasis
- Rosacea

History of other ocular conditions or CLs

- Lagophthalmos
- Blepharitis
- Meibomianitis
- Soft or hard contact lenses
### Subjective...

General systemic conditions
- Collagen vascular diseases (especially rheumatoid)
- Infectious or inflammatory diseases
- Cancers (especially lymphoma)
- Kidney disease
- Sjogren's syndrome
- Neurotropic responses (Bell's palsy)
- Thyroid (exposure) conditions

### Objective...

- No discharge present
- Excess dryness leads to reflexive aqueous tearing ("paradoxical" wet eye)
- Occasional mucoid or lipid buildup in inferior cul-de-sac
- Generally a low-grade, angular-type bulbar hyperemia
- Nonspecific papillary (palpebral) conjunctivitis
- Typical of allergic and bacterial conjunctivitis

### Objective...

- Usually less "velvety" appearing (appears dryer)
- Lid margin and inferior fornix tear menisci may be reduced (0.5 mm) or absent
- Mucoid debris (lipids, dessicated epithelial cells) may accumulate on the ocular surface or in the aqueous tear film or meniscus
- Meniscus may demonstrate "frothy" appearance
- Not uncommon to have both frothing and debris

### Objective...

- Most typical clinical sign in dry eye or keratitis sicca syndromes is SPK staining greatest in the band region of cornea and conjunctiva (exposed area of cornea and conjunctiva in palpebral fissure region)
- Common stains used:
  - Sodium fluorescein
  - Rose bengal
  - Lysamine green
Occasional dellen formations (Gaule spots)
Positive tear breakup time (TBUT) may be one of the most diagnostic considerations

Other findings to note in dry-eye diagnosis
1. Chronic conjunctivitis
2. Blepharitis and blepharoconjunctivitis
3. Meibomianitis or Meibomitis
4. Corneal epithelial abnormalities

Rule out all stimulating causes of dry-eye syndrome
1. Aggravants
2. Medications
3. Systemic causes
4. Ocular problems
5. Contact lenses

Assessment...

“Attempt” (often difficult) to classify dry eye (Holly and Lemp system)
1. Lipid layer (prevents evaporation) abnormalities
   a. Caused by infectious blepharitis or meibomitis
   b. Bacterial toxins cause rupture of tear film and secondary epithelial problems
2. Aqueous layer (thickest layer) deficiencies
   a. Lacrimal and accessory gland abnormalities
   b. Sjogren's syndrome (dry eye, dry mouth, arthritis)
   c. Drug related
   d. Neurological
3. Mucin layer deficiencies
   a. Goblet cell (conjunctival) abnormalities
   b. Drug related and Vitamin A deficiencies
   d. Stevens-Johnson syndrome
   e. Conjunctival diseases and disorders
4. Lid resurfacing (Marangoni effect) disorders
   a. Blepharitis (eg, tylosis)
   b. Lagophthalmos
   c. Colobomas (lid notching)
   d. Keratinized lid margins
   e. Trichiasis, entropion or ectropion
Assessment...
- Most common differential diagnosis is between dry-eye syndromes and anterior basement membrane disorders

<table>
<thead>
<tr>
<th>Dry Eye Syndrome</th>
<th>EBMD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mid to late day Sx</td>
<td>“Morning syndrome”</td>
</tr>
<tr>
<td>Increasing during day</td>
<td>Decreasing during day</td>
</tr>
<tr>
<td>Band SPK</td>
<td>Intraepithelial signs</td>
</tr>
<tr>
<td>Tear variations</td>
<td>- Maps, Dots, Fingerprints</td>
</tr>
<tr>
<td>+ or - Schirmer’s test</td>
<td>Schirmer’s always neg.</td>
</tr>
<tr>
<td>NaFl staining</td>
<td>NaFl staining</td>
</tr>
<tr>
<td>- &lt; 10 secs, but &gt; instant</td>
<td>- Instantaneous</td>
</tr>
<tr>
<td>- Round and enlarging</td>
<td>- Linear cascading</td>
</tr>
<tr>
<td>- Random position after blink</td>
<td>- Stationary after blink</td>
</tr>
</tbody>
</table>

Plan ...
**For Mild to Moderate Symptoms (PM or Chronic)**
- Lubricating eye drops 5 to 10 x per day
- Vitamin and mineral supplemented topical lubricants may have some nominal value in providing nutrition to the cells
  - Vitamin C and E as antioxidants
  - Vitamin B12 aids reepithelialization
  - Zinc, manganese, selenium
- Fatty fish (Omega 3 oil)
- Recheck patient in approximately 4 to 6 weeks

Plan ...
**For Moderate Conditions**
- Everything from mild treatments, plus...
- Use mucomimetic drops q 1-2 h
- Add longer-acting tear substitutes based on degree
  1. Ointments (qid to q2h)
  2. Gels
  3. Lacriserts (Merck Sharp & Dohme)
- NSAIDs (BID to QID)
- Recheck patient within 1 week

Plan ...
**For Severe Conditions**
- All moderate therapies at maximal levels, plus...
- Soft contact lens bandage therapy
  1. Use low to medium water lenses
  2. Daily wear (because of increased risk of infection)
  3. Add therapeutic drops over bandage lenses
- Additional therapies
- Punctal occlusion (collagen and silicone plugs)
- Punctal cautery (thermal or laser)
- Conjunctival flap surgical procedures
- Immunosuppressive agents
  - Steroids or cyclosporine 0.05% (*Restasis*)
“Refractive Tear Film”

- New concept from old (and new) information
- Wavefront (may be your best friend, or...!)
- The tear film and new vision and refractive information (from wavefront analysis)
- Questions we must begin to answer
- Potential uses and benefits in managing the “refractive tear film” concept:
  - Diagnostic applications
  - Therapeutic indications and applications
  - Ongoing management and market potential

Factors that effect the “refractive tear film”

- Corneal surface integrity
- Variable refractive indices of the tears
- Corneal dehydration
- Dry eye syndromes
- Evaporation
- Etc., etc., etc.

But...

Unquestionably, the most profound effect on the “refractive tear film” is the blink and it’s “Marangoni effect” on the ocular surface.

References (limited list)

“Marangoni Effect”
Motions of the surface of a liquid coupled with those of the subsurface fluid or fluids, so that movements of the liquid produce stresses in the surface and vice versa.

J. Colloid and Interface Sci. 1996

“Marangoni Effect”
- Surface flow induced by gradients in surface tension
- Mechanisms
  - Thermal gradients
  - Non-uniform evaporation patterns
  - Non-uniform solute concentrations
  - Fast evaporation in thin film
  - High surface-to-volume ratio
- Ocular surface to thin tear film
- Results in post-blink tear instability

Diagnostic and treatment potentials re: the “refractive tear film” concept
1. Improving the accuracy of routine refraction
2. Definitively assessing all eyes not correctable to 20/20
3. Assessing pre-op & post-op corneal refractive surgery patients
4. Assessing contact lens candidates for soft vs hard lens wear
5. Contact lens care including orthokeratology (e.g., CRT)
6. Expanding the use of artificial tears (beyond just lubrication)
7. Enhancing correctable vision...and
8. Approaching optimal refractive correction to 100% (20/8)

Thank you
lcatania@bellsouth.net