Eye on Biomarkers

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Biological Markers = BioMarkers

An Introduction to BioMarkers
Why this course

- Patients diagnosed with the same disease can show a spectrum of individual responses.
- Diagnostic procedures and science are catching up with the idea of custom diagnosis and therapy.

• Present the science of biomarkers in eye disease detection.
• Understand how biomarker technology is impacting eye care.
• Review patient cases where the use of biomarker mediated diagnostic technology is used for custom patient care.
An Introduction to Molecular Diagnostics

In 1998, the NIH, Definitions Working Group defined a biomarker as:

“a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention.”

Sensitivity & Specificity

Statistical measures of the performance of a binary (yes-no) classification test.

Is it a YES or a NO?

1. yes
2. yes <- maybe?
3. no <- maybe?
4. no
Sensitivity and specificity are statistical measures of the performance of a binary classification test.

**Sensitivity:**
- The true positive rate.

The proportion of actual positives which are correctly identified.

*The percentage of sick people who are correctly identified as having the condition*

**Specificity:**
- The true negative rate.

The proportion of negatives which are correctly identified.

*The percentage of healthy people who are correctly identified as NOT having the condition*

**Case 1**

40 y/o F

Complaints:
1. dry eye
2. both + signs and symptoms
3. OTC gtt 6-7 q D
4. Computer Use 8+ hrs
Aqueous Deficient Dry Eye (ADDE) vs Evaporative Dry Eye (EDE)

1. Conventional test: Schirmer, TBUT, Stains
2. Tear Osmolarity
3. lid margin observation
4. Non Invasive: NITBUT, Lipiview
5. OSDI score: 67

Inflammation:

- Pro-inflammatory cytokines and inflammatory markers (Lactoferrin - MMP9 - Lysosomes - Tear Lipocalin) are secreted by the lacrimal gland, which further damage the ocular surface and start an inflammatory cascade. [1]

- Inflammation is largely attributed to a metabolic breakdown of lipids in the meibomian glands, with fatty acids obstructing the glands and hindering their function. (EDE)

- MMP-9 is a more sensitive diagnostic marker for dry eye than clinical signs alone.¹

- Inflammation is present before the clinical signs of dry eye.²

- Increased MMP-9 activity in dry eyes may contribute to deranged corneal epithelial barrier function, increased corneal desquamation, and corneal surface irregularity.³


3. RPS InflammaDry positive agreement and negative agreement was compared to clinical truth in RPS clinical study: protocol #1 2-0615.

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- Sensitivity 85%

- Specificity 94%

- Does our patient have an inflammatory component to her dry eye?
Positive RPS
Aqueous Deficient Dry Eye (ADDE)

- Patient Management:
  - Loteprednol Gel 0.5% qid for 2 weeks, bid for 2 weeks
  - Cyclosporine A 0.05% emulsion - bid
  - Artificial Tears BID / PRN

Case 1
40 y/o F

Accurate diagnosis provides a better treatment and personalized plan
Case 2
66 y/o M

Complaints:
1. Watery eyes
2. Using OTC gtt bid
3. Computer Use 8+ hrs
4. OSDI score: 62
5. ECCE in 3 weeks

Pre-Surgical surface treatments are linked to lower inflammation, improved vision and surgical outcomes

Evaporative Dry Eye (EDE)
Aqueous Deficient Dry Eye (ADDE) vs Evaporative Dry Eye (EDE)

RPS test: negative

WE KNOW:
it is not inflammatory

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Case 2
66 y/o M
Aqueous Deficient w/o Inflammation

PF Lubricant
Lid Scrubs
Low BAK AntiHistamine
Have a Martini!

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Red Eye? what type?
Yeah remember that list?

- HSV
- Chlamydia
- Bacterial Conjunctivitis (including GC in neonate)
- Toxic conjunctivitis (molliccum)
- Allergic conjunctivitis
- Atopic conjunctivitis
- Contact Lens related complications
- Blepharoconjunctivitis
- Foreign body
- Pinkeye's ocularconjunctival syndrome
- Cat-scratch disease (Bartonella Henselae)
Acute Conjunctivitis

- 6 MM cases in the US each year
- 3 major subtypes
  - Allergic
  - Bacterial
  - Viral
- Similar clinical presentation among the 3
- Studies indicate that ECPs make an accurate diagnosis nearly 50% of the time

Overlapping Signs & Symptoms

- Redness
- Peeling/discharge
- Lids:
  - Edema
  - Inflamed
- Eyelash:
  - Irritation
  - Foreign body sensation
- Eyelid:
  - Edema
- Discharge:
  - Clear
  - Yellow
  - Serous
- Watery eyes
- Itching
- Sensation: gritty or foreign body

References:

Case #3

1. Red eye
2. Watery during the day and crusting noted in the mornings
3. Swollen lids
4. One eye first, later spread to the opposite eye
5. No itch
AdenoPlus®

- Detects all known serotypes of Adenovirus
- Easy to use – can be performed by a nurse or technician
- In-office (point-of-care) test
- Low cost – no additional equipment required
- One time use – disposable
- Minimal amount of virus antibody needed for detection
  - Only 6 ng/ml
- Reimbursable under CPT code 87809 QW
- CLIA - www.CMS.gov

Fast
- ≤ 2 minutes to complete test, results in 10 minutes or less

Accurate
- Identifies Adenovirus with 90% sensitivity and 96% specificity

Easy
- Completed in 4 simple Steps

Case #3

1. Red eye
2. Watery during the day and crusting noted in the mornings
3. Swollen lids
4. One eye first, later spread to the opposite eye
5. No itch
Adenovirus!

- EPIDEMIOLOGY
  - extremely common in the US
  - occurs equally in men and women
  - no racial predilection
  - highly contagious—outbreaks can sometimes be traced to infected individuals or locations

- Represents the most common external ocular infection
- 1 out of every 4 cases of Acute Conjunctivitis seen by eye care professionals is caused by adenovirus
- Most frequent virus isolated from the conjunctiva
- Prevalence varies based on time of year and geographic location
- 20-70% of all conjunctivitis cases are viral up to 90% of these may be Adenovirus

Adenovirus!

- Can live on inanimate surfaces for 4-5 weeks
- Stable to adverse chemical and physical conditions
- Can shed for 14-16 days after initial symptoms (contagious!), continued immune stimulus
- Common modes of transmission:
  - Hand-to-eye
  - Airborne respiratory droplets


Case 3
Adenoviral

Treatment options:

1. OTC - Palliative
2. Betadine 3-5% wash (3x anesthetic+NSAID - 1 min irrigation + NSAID)
3. Ganciclovir gel 0.15% 5 x day - 10 d
4. Isolation (?)

Case #4

1. Red eye
2. Watery during the day and crusting noted in the mornings OU
3. Swollen lids
4. Occasional itch
5. + FB sensation
Case #4

“Si no es Juan es Pedro!”

(A NON approved but very common Puertorrican Differential Dx technique)

THE RED EYE PROTOCOL
for conjunctivitis

1. Use a "tip and dip" motion to dip the tip of the swab into the specimen container (cover removed) to collect a tear sample.
2. Secure the sample collector to the eye, CAUTIOUSLY, and press firmly where indicated.
3. Dip the test cassette into the provided buffer until the 20 seconds. Replace the cap.
4. Read the result 2 times (1 red, 1 white square). 

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Case #4

Virus
Bacteria
Allergy

M
Case #4 allergy
Treatment options:

OTC ?
Rx Antihistamines

Myths of Sjögren’s

• “All Sjögren’s patients are identified and diagnosed”
• “There are only a few patients in my practice”
• “Nothing can be done for the patients if they are diagnosed”
• “Sjögren’s syndrome does not have serious long-term consequences, it is just a nuisance”

Impact of Sjögren’s Syndrome

Sjögren’s syndrome is a chronic autoimmune disease in which a person’s white blood cells attack their moisture-producing glands.
Dry Eye Patients & Sjögren’s Syndrome

- More than 25 MM patients with dry eye in the US
- At least 4 MM patients with Sjögren’s syndrome
- As many as 1 in 10 patients with dry eye have undiagnosed Sjögren’s syndrome
- Patients with dry eye symptoms see their Eye Care Practitioner first

Eye Care Professionals are uniquely positioned to play a pivotal role in helping to identify undiagnosed Sjögren’s patients

Early Detection of Sjögren’s Syndrome

- Advanced Diagnostic Test Panel
  o Includes 4 traditional and 3 new proprietary biomarkers
  o Detects Sjögren’s significantly earlier than previous tests
  o Increased sensitivity & specificity compared to other test methods
- Convenient, in-office kit used to collect patient specimen
Case 1

40 y/o F

Complaints:
1. dry eye
2. both + signs and symptoms
3. OTC gtt 6-7 q D
4. Computer Use 8+ hrs

Case 1

26 y/o F + Sjogren's

Rheumatologist consult
spoke with PCP
Use Universal precautions!

- Wear gloves
- Wash hands
- Dispose of collectors in biohazard bag/container
- Clean surface(s)
- OSHA compliance
  - manuals - instructions

Take home:
- Recognize the use of BioMarkers - we will see more in the future.
- A negative test will give you information too.
- Diagnostic testing is changing and will change providing safer and accurate diagnosis of eye disease.

Thank You!
Q and A