Integrating Laboratory Testing Into Your Optometric Practice
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Disclosure Statement: Nothing to disclose

The role of laboratory testing in the optometric practice.....
- Ordering the tests
- Co-managing
- In-office tests
  - “point of care” testing
- Considerations
  - Effect on your management plan
  - Rapidity of results
  - Patient convenience
  - Financial/practical considerations

Requests for Outside lab tests/
Working with a local laboratory
- Considerations:
  - Quality of test procedures
  - Frequency and timeliness of specimen pickup and delivery of results
  - Is there an onsite consultant pathologist to help interpret results or explain procedures?
  - Are supplies (such as slides, culturettes, and specimen containers) provided free of charge to your office?
  - Does the lab bill patients or insurance companies directly?

If YOU order the tests...
- Interpret
- Laboratory Tests and Diagnostic Procedures
  - 6th edition - 2013
  - Chernecky and Berger
    - Includes Herbal interactions
- Communicate
- Treat
- Refer

Who regulates laboratory testing?
- Clinical Laboratory Improvement Amendment (CLIA)
  - enacted in 1992
  - Administered by Federal CMS
  - Regulates all facilities that test human specimens for the purpose of diagnosis, treatment or monitoring
- Other regulatory bodies
  - State Law
  - OSHA
  - Food & Drug Administration
    - Approves tests marketed commercially
    - CDC determines, with FDA, test categorization
Before performing in-office laboratory tests:

- You must be CLIA-certified
  - Certificate of Waiver (Form CMS-116)
- Obtain patient consent

**CLIA-Waived Tests**

<table>
<thead>
<tr>
<th>Waived</th>
<th>Moderate</th>
<th>High Complexity</th>
</tr>
</thead>
</table>

- Waived tests are defined as:
  - "simple laboratory examinations and procedures that have an insignificant risk of an erroneous result, or pose no reasonable risk of harm to the patient if performed incorrectly"
- Still subject to
  - Applicable fees
  - CLIA inspections

**Billing for in-office lab procedures**

- Medical necessity must be documented
- Advanced Beneficiary Notice (ABN)—have patient sign one
- CPT codes for CLIA-Waived tests
  - –QW modifier at the end
  - check local requirements

"Blood work-up"....tests driven by differentials

- CBC with differential
- FBS
- Chem 7
- Lipid Profile
- ESR
- C-Reactive Protein
### CBC Index

<table>
<thead>
<tr>
<th>CBC Index</th>
<th>Clinical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red Blood Count (RBC)</td>
<td>Anemia and classification</td>
</tr>
<tr>
<td>Platelet Count (PLT)</td>
<td>Clotting disorders</td>
</tr>
<tr>
<td>Mean Platelet Volume (MPV)</td>
<td>Clotting disorders</td>
</tr>
<tr>
<td>White Blood Count (WBC) with Differential</td>
<td></td>
</tr>
<tr>
<td>Neutrophils</td>
<td>↑ in Leukemia, ↓ in Leukopenia (granulomatous dz, meds, bacterial inf)</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>↑ in viral infections</td>
</tr>
<tr>
<td>Monocytes</td>
<td>↑ in bacterial infections</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>Involved in allergic disorders and parasitic infections</td>
</tr>
<tr>
<td>Basophils</td>
<td>Immediate immune reactions</td>
</tr>
<tr>
<td>Hemoglobin (Hb)</td>
<td>Anemia and classification</td>
</tr>
<tr>
<td>Hematocrit (Hct)</td>
<td>↑ in PCV, CHF, COPD, ↑ altitude</td>
</tr>
</tbody>
</table>

### RBC Indices

- Mean Corpuscular Volume (MCV): ↑ in pernicious anemia | ↓ in Fe deficiency anemia
- RBC Distribution Width (RDW): |
- Mean Corpuscular Hemoglobin (MCH): |
- Mean Corpuscular Hemoglobin Concentration (MCHC): ↑ Hyperchromic (B12 and Folic Acid Def) | ↓ Hypochromic (Fe Def, thalassemia)

### Basic Metabolic Panel (aka “Chem 7”)

1. Creatinine
2. Blood urea nitrogen (BUN)
3. Glucose
4. Carbon dioxide
5. Chloride
6. Sodium
7. Potassium
8. (Sometimes Calcium)

- Screens for
  - Kidney disease
  - Liver Disease
  - Diabetes and other blood sugar disorders

### In-office Glucometry

**Blood glucose reading in ~5 seconds**

**Indications**
- Suspicion of diabetes
- Diabetic with poor control
- Diabetic who isn’t feeling well

**Normal values:**
- Fasting <126 mg/dL
- 100-125 is “prediabetes” or borderline
- Random <200 mg/dL

**Case #1: No Hx Diabetes but Retinal Changes**

- 39 AA Female
- FHx diabetes but none reported
- Overweight
- LPE: 7 years ago

**Billing for Glucometry**

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>E2362QW</td>
<td>Glucometry (at-home device)</td>
</tr>
</tbody>
</table>

- **Average Reimbursement**: $3.42
- **ICD Codes**: Most codes corresponding to previously diagnosed diabetes, specifically uncontrolled
  - Other Considerations: Covered once per month

**Current ADA Diagnostic Criteria**

- Random plasma glucose ≥ 200mg/dL + symptoms (polyuria, thirst, wt loss, blurred vision)
- Fasting plasma glucose ≥ 126mg/dL
- OGTT 2 hour post-load glucose ≥ 200mg/dL
- HbA1c ≥ 6.5%
In-office HbA1c Testing

- **A1C Now+® (PTS Diagnostics)**
  - 99% lab accuracy
  - Results in 5 minutes
  - no fasting required
  - www.a1cnow.com

- Cost: ~$12.00/test (available in sets of 10 or 20)

Billing for HbA1c using A1cNow+

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>A1cNow+®</th>
</tr>
</thead>
<tbody>
<tr>
<td>83037QW</td>
<td>A1cNow+®</td>
</tr>
</tbody>
</table>

- Average Reimbursement: $118
- ICD Codes: Most codes corresponding to previously diagnosed diabetes
- Other Considerations: Once per 3 months

Hemoglobin A1c and retinopathy

- Diabetes Control and Complications Trial (DCCT): A 1% reduction lowers the risk of serious complications by 40%.
- United Kingdom Prospective Diabetes Study (UKPDS): A 1% reduction lowers the risk of microvascular complications by 37%.

Estimated Average Glucose: an alternative to A1c

- (28.7 x A1c) – 46.7 = eAG
- Comparison of A1c and eAG levels:

<table>
<thead>
<tr>
<th>A1C%</th>
<th>eAG (mg/dL)</th>
<th>eAG (mmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6%</td>
<td>126</td>
<td>7.0</td>
</tr>
<tr>
<td>6.5%</td>
<td>140</td>
<td>7.8</td>
</tr>
<tr>
<td>7%</td>
<td>154</td>
<td>8.6</td>
</tr>
<tr>
<td>7.5%</td>
<td>169</td>
<td>9.4</td>
</tr>
<tr>
<td>8%</td>
<td>183</td>
<td>10.3</td>
</tr>
<tr>
<td>8.5%</td>
<td>197</td>
<td>10.9</td>
</tr>
<tr>
<td>9%</td>
<td>212</td>
<td>11.8</td>
</tr>
<tr>
<td>9.5%</td>
<td>226</td>
<td>12.6</td>
</tr>
<tr>
<td>10%</td>
<td>240</td>
<td>13.4</td>
</tr>
</tbody>
</table>

ABCs of Diabetes

- A – A1C/blood glucose is “individualized”
- B – 140/80 or less
- C – LDLs 100 or <70 if CVD
- D – Diet
- E – Exercise – 150 min per week
- S – Smoking increases risk of retinopathy

Case #2: The red eye

- A 17-year old Caucasian male presents complaining of red, irritated, watery eyes. He states that it began in the right eye about 4 days ago but has since moved into the left eye as well. He denies having any recent cold or flu and is not a contact lens wearer. Best-corrected visual acuity is 20/30+2 OD and 20/20-1 OS. Subtle petechial conjunctival hemorrhages and sub-epithelial infiltrates were noted on slit lamp examination OD>OS.
Think back 10 years ago...
- Usually a clinical diagnosis
- Misdiagnosis in 50% of all cases^{1,2}

Lab diagnosis includes:
- Virus isolation in cell culture
  - Gold standard
  - 3-21 days for results
- Polymerase chain reaction (PCR)
  - Expensive
  - 2-4 days for results


And now...
- STILL mostly a clinical diagnosis
- CLIA-waved
- www.rpsdetectors.com
- Results in 10 minutes
- Uses a small tear fluid sample
- Identifies all 51 serotypes of adenovirus
- Anesthetic okay to use

What can we gain from this??
- Clinical Benefits:
  - ↑ accuracy of dx and instituting proper tx
  - ↓ empirical treatment and unnecessary antibiotic use
  - Reinforces patient acceptance of palliative treatment
  - Limits spread of disease

<table>
<thead>
<tr>
<th>Publication</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sambursky R, JAMA Ophthalmol 2013</td>
<td>85%</td>
<td>98%</td>
</tr>
<tr>
<td>Kam, KYR, et al. Br J Ophthalmol 2015</td>
<td>39.5%</td>
<td>95.5%</td>
</tr>
</tbody>
</table>

And: PCR was positive for chlamydia in 4% of cases, suggesting that PCR is indicated...

Betadine
- povidone-iodine ophthalmic solution
  - (85:15)
- broad-spectrum disinfectant
- off-labeled use
Betadine
- Informed consent
- Anesthetic
- 1-2 drops betadine
  - Treat both eyes!!
- Swab lids
- Irrigate well
- Topical NSAID
- Conjunctival staining lasts only a couple of hours

Billing for AdenoPlus - RPS

<table>
<thead>
<tr>
<th>ICD Codes</th>
<th>AdenoPlus®</th>
</tr>
</thead>
<tbody>
<tr>
<td>H10.31[2,3] - Acute conjunctivitis, unspecified</td>
<td></td>
</tr>
<tr>
<td>H10.021[2,3] - Other mucopurulent conjunctivitis</td>
<td></td>
</tr>
<tr>
<td>H10.9 — Conjunctivitis, unspecified</td>
<td></td>
</tr>
<tr>
<td>B30.1 - Conjunctivitis due to Adenovirus</td>
<td></td>
</tr>
<tr>
<td>B30.9 — Viral conjunctivitis, unspecified</td>
<td></td>
</tr>
</tbody>
</table>

The future of conjunctivitis?
- IgE Detector
- HSV Detector
- Chlamydia Detectors
- Multi-pathogen detectors
- Adeno-HSV Duo-Detectors

- Topical anti-virals for treatment against adenovirus currently in clinical trials

Case #3: 46 WF -- MISERABLE
- Chroniclly moderate to severe dry eye symptoms

- Hx of:
  - Continued AT therapy
  - Smart Plugs
  - Restasis x 2 tries
  - Fuch’s – on Muro
  - Dry mouth
  - Joint pain
  - Skin involvement
Sjögren's Syndrome Tests

- Tests for classic and new inflammatory markers for Sjögren's
  - SS= syndrome, SD=disease
    - Ro
    - La
    - SP-1
    - CA6
    - PSP
    - Classic markers: 20-30% are (-)
    - Newly identified markers – often present in symptomatic patients when classic markers are not
  - Up to 60% specificity / sensitivity
  - Earlier Dx – before organ damage

Sample Collection

- No CLIA waiver needed
- No billing

Sjö test can identify patients early...

- Estimated to affect 4 million people in the US
  - 3 million undiagnosed
- Generally diagnosed in late stages
  - Glands are already destroyed
  - Patients often asymptomatic until then
  - Palliative tx

Tear Composition

- Tonicity
  - TearLab
    - Measures osmolarity of small volume (50nL) of tears
    - Dry ≥308 mOsm/L
    - Difference ≥8 mOsm/L between eyes also clinically significant

Tear Film Osmolarity

- Increase in osmolarity associated with DE
  - ↓ tear production and ↑ evaporation: less fluid
  - Indicates a failure of homeostatic regulation
  - ↑ ocular surface damage, ↑ inflammation

TearLab™ Osmolarity

- Quantitative -- Increase in patient understanding of disease state/severity
  - Perform before other tests/drops/dyes/anesthetics – affected by reflex tearing
  - Can fluctuate with progression/regression
Best for Early Diagnosis of DED

- Important and effective indicator of DED
  - Up to 73% sensitivity and 90% specificity

- Early indication of DED
  - 64-67% sensitive for mild DED

Dry Eye Disease and MMP-9

Matrix metalloproteinases (MMP) are proteolytic enzymes that are produced by stressed epithelial cells on the ocular surface

- MMP-9 in Tears
  - Non-specific inflammatory marker
  - Ocular surface disease (dry eye) demonstrates elevated levels of MMP-9 in tears¹
  - Normal range between 3-41 ng/ml
  - Elevated MMP-9 often precedes other findings – up to 57% with symptoms have no signs


InflammaDry®

- Perform before any drops
- Much like AdenoPlus – dabbing vs. dragging
  - Release lid for blinking after 2-3 dabs
  - Repeat 6-8 times
  - Let sample pad rest on conj for 5 sec to saturate
  - Any pink at all = positive
  - No blue line = invalid test

InflammaDry® Results

Normal levels of MMP-9 in human tears ranges from 3-41 ng/ml

Positively Tested

<table>
<thead>
<tr>
<th>MMP-9 ≥ 40 ng/ml</th>
<th>MMP-9 &lt; 40 ng/ml</th>
</tr>
</thead>
</table>

Billing for InflammaDry® - RPS

<table>
<thead>
<tr>
<th>Test</th>
<th>Reimbursement</th>
</tr>
</thead>
<tbody>
<tr>
<td>RPS</td>
<td>$15.70</td>
</tr>
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ICD Codes

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tr>
<td>H04.121</td>
<td>Dry eye, lacrimal gland OD, OS, OU</td>
</tr>
<tr>
<td>H16.21</td>
<td>Exposure keratoconjunctivitis</td>
</tr>
<tr>
<td>H16.221</td>
<td>- KC, not Sjögrens OD, OS, OU</td>
</tr>
<tr>
<td>M35.01</td>
<td>Sicca syndrome with keratoconjunctivitis</td>
</tr>
<tr>
<td>H11.141</td>
<td>Conjunctival xerosis OD, OS, OU</td>
</tr>
</tbody>
</table>

Billing for TearLab™ Osmolarity

<table>
<thead>
<tr>
<th>Test</th>
<th>Reimbursement</th>
</tr>
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<tbody>
<tr>
<td>RPS</td>
<td>$22.34</td>
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4/8/2017
What does this add to the clinical picture?
- Other dry eye testing has limitations
- Signs/symptoms of DES often disagree
- Inflammation can alert you to underlying cause
- Aids in initial dx and guide for management

![Inflammation Table]

Case #4: 46 yo AA female
- What is your diagnosis?
- Is a lab workup needed?
- What laboratory tests to you want to order?
- What is the relevance of these laboratory tests?

Lab Testing in Anterior Uveitis
- WHEN DO YOU PULL THE TRIGGER?
  - Era of “shotgun” approach to laboratory testing has passed
  - Order appropriate tests based on clinical picture
- Freebie if...
  - First occurrence
  - Acute
  - Mild
  - Unilateral
  - Nongranulomatous

Keep in Mind... (useful patterns)
- 38-56% of cases of anterior uveitis are idiopathic
- Acute, recurrent, unilateral (may be alternating eyes) anterior uveitis... 50-80% are spondyloarthropathies...order HLA-B27
- Look closely for evidence of herpetic infection (iris, cornea)
- Think sarcoidosis if chronic granulomatous
- Have a suspicion about syphilis – include it if ordering laboratory testing
- Refer as appropriate

Anterior Uveitis
- Non-Granulomatous
  - Acute or chronic, painful
  - Circumlimbal flush
  - Moderate to severe presentation
  - Normal keratic precipitates (KPs)
  - More cell, less flare
  - Mild to moderate posterior synchiae
  - Choroidal involvement rare

- Granulomatous
  - Chronic, insidious
  - Minimal injection
  - Milder presentation
  - Mutton fat keratic precipitates (KPs)
  - Less cell, more flare
  - Heavy posterior synchiae
  - Posterior involvement common
  - Koeppe and Busacca nodules
  - Rarely, if ever, idiopathic!

Common etiologies of Anterior Uveitis
- Non-Granulomatous
  - Acute
  - Idiopathic
  - Ankylosing Spondylitis
  - Crohn’s disease
  - Reactive Arthritis (formerly known as Reiter’s syndrome)
  - Lyme disease
  - Herpes simplex or zoster
  - HIV/AIDS
  - Postoperative
  - Trauma
  - Chronic
  - Juvenile rheumatoid arthritis (JRA)

- Granulomatous
  - Sarcoidosis
  - Tuberculosis
  - Syphilis
Sarcoidosis
- Sarcoidosis is a multisystemic granulomatous disease of unknown etiology
  - 95% have pulmonary involvement
  - Ocular manifestations in 20-25%
- Definitive diagnosis requires chest x-ray along with a tissue biopsy
- Lab testing: ACE, Serum Lysosome

If both ACE & Serum Lysosome are elevated, positive predictive value of 83% for Sarcoidosis

Syphilis
- Multisystem disease caused by the spirochete Treponema pallidum
- Screening Tests (detect active disease): VDRL, RPR
- Diagnostic Tests (detect a history of disease): FTA-ABS, MHA-TP
- Order one screening and one diagnostic test

Interpretation of Tests

<table>
<thead>
<tr>
<th>RPR/VDRL</th>
<th>FTA-ABS/MHA-TP</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>+</td>
<td>Active syphilis</td>
</tr>
<tr>
<td>-</td>
<td>+</td>
<td>Adequate treatment</td>
</tr>
<tr>
<td>+</td>
<td>-</td>
<td>False positive</td>
</tr>
<tr>
<td>-</td>
<td>-</td>
<td>No exposure or recent exposure</td>
</tr>
</tbody>
</table>

Case #5: 61 Year old WM—sudden vision loss
- 20/60
- Hx – headache
- Pupils – normal
- Inferior VF loss
- Sectoral optic disc edema
- Disc hemorrhage
Considering the Differentials....

**Giant cell?**
- Age 61
- Headache
- Swollen disc
- Acute loss of vision

**Non-arteritic?**
- Vision is only 20/60
- Pupils are normal
- Disc is not waxy/chalky-pale

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**Anterior Ischemic Optic Neuropathy**

**Arteritic – 5%**
- Fellow eye involvement: 75% within 6-8 weeks
- Inflammation elastic tissue of vessel wall
- Visual prognosis much worse
- 1 in 5 patients do not manifest systemic symptoms

**Non-Arteritic – 95%**
- Fellow eye involvement: 15-35% within 7 mos
- Perfusion pressure ratio imbalance

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**Order the labs anyway!**

- Westergren ESR
- C-Reactive Protein
- CBC and platelet count

- When the suspicion is strong.....
  - IV/oral steroids (60-80 mg oral prednisone qd)

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**Erythrocyte Sedimentation Rate**

- Non-specific marker of inflammation
- Rate at which red blood cells settle in anti-coagulated blood in 1 hour
- Inflammatory conditions alter proteins – RBCs are heavier, settle quicker

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**Blood Sample Collection**

- Using transfer pipette, fill reservoir to filling line
- Firmly push Dispette tube into reservoir, penetrating the cap membrane
...exactly one hour later

Erythrocyte Sedimentation Rate (ESR)
- Normal values for Westergren ESR
  - Males: age/2
  - Females: (age+10)/2
- Always order a CBC with ESR, as anemia can falsely increase the ESR

C-Reactive Protein (CRP)
- Protein produced by the liver in response to injury/inflammation
- Reduces rapidly after inflammation subsides
- Normal is ≤2.45 mg/dl
- Elevated with
  - Infection
  - Fever
  - Arthritis
  - Myocardial infarction
  - Malignancies

Considerations
- Both ESR and CRP are elevated with systemic inflammation
- 13% of GCA patients have normal ESR!
- ESR + CRP offers 97% specificity for GCA (Hayreh 1998)
- Anemia can falsely elevate ESR – always order CBC

In Summary...
- Ordering the tests
- In-office tests
- Consider...
  - Potential effect on your management plan
  - Efficiency, practicality and patient convenience