Improving Ordering and Interpretation of Laboratory Tests: A Reference Lab Perspective

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Presentation Overview

- Problems with current lab diagnosis model
- Solutions
  - Pull (online resources)
  - Push (customized reporting)
  - Analytics (customized feedback)
  - Structural changes (changing the rules)
Laboratory Diagnosis

MD sees patient

MD orders test

Lab obtains specimen

Test performed

Lab issues result

MD interprets result

Laboratory Testing
Lab Tests Available in Clinical Practice

- **1956**: 500 tests
- **2006**: 2500 tests
Variation in Utilization

• Study at 17 Academic Medical Centers
• Lab costs in highest quintile were 82% higher than in lowest quintile
• Lab costs varied more than any other cost category
• No measurable difference in outcomes

• Fisher et al. Health Affairs 2004
Errors in Laboratory Testing

• Between 5% and 50% of all inpatient lab test orders are inappropriate.

• Van Walraven and Naylor, JAMA 1998
Impact of Clinical Laboratory Testing

- ~2% of health care budget
- Drives >50% of major healthcare decisions

Quality impact is out of proportion to direct cost impact!
Downstream Effects of Health Services per Dollar Spent

- Lab Tests
- Meds
- Disposables
Ulysses Syndrome

- Phenomenon whereby one unnecessary test leads to a long sequence of unnecessary followup testing and/or therapy.
- Typically occurs when a test result is slightly outside the reference interval or represents a normal variant.

Overall appropriateness of Free PSA orders based on age, tPSA

Appropriate 49%

Inappropriate 51%

Jackson BR, Roberts WR. J Gen Int Med 2005 Sep;20(9):859-61
Thrombophilia Testing: Orders for First vs. Second Line Tests

% of tests that are first-line

- Antithrombin
- Protein S
- Protein C
- V Leiden

- All clients
- Only clients ordering both (or all three) tests
Improved Test Ordering: Impact on Patients

- Faster, more accurate diagnosis
- More appropriate therapy
- Shorter hospital stays
- Fewer doctor visits
- Better health
- Better satisfaction
Improved Test Ordering: Impact on Hospitals

• More accurate diagnosis = higher quality of care
• Fewer inappropriate/unnecessary tests
  - shorter lengths of stay
  - fewer outpatient visits
  - fewer unnecessary procedures
• Currently, HMO’s have more to gain than fee-for-service
• Medicare pay-for-performance will create new incentives for quality
MD sees patient

MD orders test

Lab obtains specimen

Test performed

Lab issues result

MD interprets result

Laboratory Testing
Is it Possible to Change Physician Behavior?

• Of course -- drug companies have proven this clearly
  1. Give doctors fast, easy access to information they need (Pull)
  2. Optimize pathology reports (Push)
  3. Actively monitor utilization and provide feedback (Analytics)
  4. Structural changes (Rules)
Pull: Easy access to trusted information

- Pathologist on call service
  - Necessary but not sufficient
  - Fast turnaround time
  - Accurate, clinically useful responses

- Use as learning opportunity
  (how are we not meeting physicians’ information needs?)
Pull: Easy access to trusted information

- Online test directories
  - Optimize for physicians, not just office staff
  - Link to ordering and interpretive guidance
- Disease context
- Related tests
- Clinical guidelines
- Etc.
ARUP Consult™, Version 1.2, is a dynamic tool that provides instant, point-of-care access to ordering and interpreting hundreds of laboratory tests:

- Over 1,000 lab tests categorized for diagnostic decision making
- Disease-specific topics include background information, test ordering suggestions, and concise diagnostic advice
- Co-authored and maintained by ARUP's expert panel of medical faculty and consultants
- Recommendations congruent with national guidelines
- Diagnostic algorithms available
- Automatic updates for PDA and Web platforms

Provide feedback on ARUP Consult
For questions, write to arupconsult@arulab.com.
Celiac Disease

CLINICAL BACKGROUND

Gluten sensitive enteropathy (GSE) is non-allergic hypersensitivity to gluten or storage proteins found in wheat and other cereals.

- Hypersensitivity causes intestinal villous atrophy (flattening) and malabsorption
- Celiac disease and dermatitis herpetiformis are recognized forms
- Patient may be asymptomatic

Symptoms
- Diarrhea
- Gastrointestinal problems
- Anemia
- Fatigue
- Psychiatric problems
- Other diverse side effects
  - Dermatitis herpetiformis
  - Increased risk of lymphoma
## INDICATIONS FOR ORDERING

<table>
<thead>
<tr>
<th>Test Name and Number</th>
<th>Recommended Use</th>
<th>Limitations</th>
<th>Follow Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Celiac Disease</td>
<td>Order when gluten sensitivity suspected in patient with chronic diarrhea Preferred Panel for celiac disease diagnosis (Panel includes IgA, tissue transglutaminase antibodies, and gliadin peptide antibodies)</td>
<td>Test results alone are not diagnostic. Use in conjunction with other clinical findings and biopsy to make diagnosis of celiac disease/gluten sensitive enteropathy. Many children under 3 do not make tissue transglutaminase or endomysial antibodies well which results in false-negative test results; test for anti-IgG and IgA gliadin</td>
<td></td>
</tr>
<tr>
<td>Reflexive Panel</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0051065</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immunoglobulin A</td>
<td>First step in celiac diagnostic algorithm; IgA results determine whether to use IgA or IgG versions of subsequent tests</td>
<td>Test results alone are not diagnostic. Use in conjunction with other clinical findings and biopsy to make diagnosis of celiac disease/gluten sensitive enteropathy. Many children under 3 do not make tissue transglutaminase or endomysial antibodies well which results in false-negative test results; test for anti-IgG and IgA gliadin</td>
<td></td>
</tr>
<tr>
<td>A, Serum</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0050340</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Celiac Disease/Gluten Sensitive Enteropathy Testing

INDICATIONS FOR TESTING

Symptomatic individuals
- Nonspecific symptoms (anemia, diarrhea, failure to thrive, fever, skin rash and weight loss)
- Diarrhea of more than 4 weeks duration

Asymptomatic individuals with:
- Celiac disease in first degree relatives
- Autoimmune disease associated with celiac disease (type I diabetes, autoimmune thyroiditis, etc.)
- Non-autoimmune conditions associated with celiac disease (Down syndrome, Turner syndrome, etc.)

Immunoglobulin A, Serum 0050340

If IgA is <7 mg/dL
- Tissue Transglutaminase Antibody, IgG 0066009
- positive → Consistent with celiac disease
- negative → AGE
  - Patient is ≥ 3 years old

If IgA is ≥7 mg/dL
- *Tissue Transglutaminase Antibody, IgA 0097709
- positive → Consistent with celiac disease
- negative → AGE
  - Patient is < 3 years old
Push: Optimized reporting

• Report formats
  - HL7 (and most EMR systems, for that matter) designed with discrete single values in mind
    • Sodium, glucose, etc.
  - HL7 and EMR’s terrible at integrating complex data involving multiple tests
    • HIV genotypes, etc.
Push: Optimized reporting

• Formatted integrated reports that doctors find easy to read
  - Can’t distribute over most HL7 interfaces; requires paper, proprietary network and/or web distribution

• Billed pathologist consultations
  - Useful model for complex coag testing
  - Jury still out on broader applicability
# VircoTYPE HIV-1

## The Complete Resistance Analysis

### Patient/Sample Details

<table>
<thead>
<tr>
<th>Patient name</th>
<th>HIV, VT10</th>
<th>Sample ID</th>
<th>0504600200</th>
<th>Client ID:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient ID</td>
<td>0504600200</td>
<td>Collection Date</td>
<td></td>
<td>Physician:</td>
</tr>
<tr>
<td>MRN</td>
<td>Received by Virco on Feb 23, 2005</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date of birth</td>
<td>Visit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Virco ID</td>
<td>ASP00000028</td>
<td>Report date</td>
<td>Feb 23, 2005</td>
<td></td>
</tr>
</tbody>
</table>

### SUMMARY REPORT

#### DRUGS

<table>
<thead>
<tr>
<th>DRUGS</th>
<th>FOLD CHANGE</th>
<th>CUT-OFF (BCO - CCO)</th>
<th>RESISTANCE ANALYSIS</th>
<th>CLINICAL NOTES</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRTI / NtRTI * mutations 67N, 70R, 184V, 211K, 219E</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retrovir®</td>
<td>Zidovudine</td>
<td>2.6</td>
<td>4.0</td>
<td>SUSCEPTIBLE</td>
</tr>
<tr>
<td>Epivir®</td>
<td>Lamivudine</td>
<td>45.7</td>
<td>4.5</td>
<td>RESISTANT</td>
</tr>
<tr>
<td>Videx®</td>
<td>Didanosine</td>
<td>1.2</td>
<td>2.0</td>
<td>SUSCEPTIBLE</td>
</tr>
<tr>
<td>Hivid®</td>
<td>Zalcitabine</td>
<td>1.4</td>
<td>2.0</td>
<td>SUSCEPTIBLE</td>
</tr>
<tr>
<td>Zerit®</td>
<td>Stavudine</td>
<td>0.9</td>
<td>1.75</td>
<td>SUSCEPTIBLE</td>
</tr>
<tr>
<td>Ziagen®</td>
<td>Abacavir</td>
<td>1.8</td>
<td>3.0 - 3.2</td>
<td>SUSCEPTIBLE</td>
</tr>
<tr>
<td>Emtriva™</td>
<td>Emtricitabine</td>
<td>55.0</td>
<td>4.5</td>
<td>RESISTANT</td>
</tr>
<tr>
<td>Viread™ (*)</td>
<td>Tenofovir DF</td>
<td>0.7</td>
<td>3.0</td>
<td>SUSCEPTIBLE</td>
</tr>
</tbody>
</table>
## GENOTYPE WITH QUANTITATIVE PHENOTYPIC ANALYSIS

### ANAlysed Sequence Region
- **PRO 1-99**
- **RT 1-335**

### Subtype Analysis
- **Clade B**

### Drugs

<table>
<thead>
<tr>
<th>NRTI / NtRTI * mutations 67N, 70R, 184V, 211K, 219E</th>
<th>Matches in Database</th>
<th>Proportion of Matched Samples</th>
<th>Cut-off Values</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Retrovir®</strong></td>
<td>Zidovudine AZT 887</td>
<td>within normal susceptibility range</td>
<td>2.6 4.0</td>
</tr>
<tr>
<td><strong>Epivir®</strong></td>
<td>Lamivudine 3TC 968</td>
<td>above normal susceptibility range</td>
<td>45.7 4.5</td>
</tr>
<tr>
<td><strong>Videx®</strong></td>
<td>Didanosine ddI 728</td>
<td>above normal susceptibility range</td>
<td>1.2 2.0</td>
</tr>
<tr>
<td><strong>Hivid®</strong></td>
<td>Zalcitabine ddC 150</td>
<td>above normal susceptibility range but below clinical cut-off</td>
<td>1.4 2.0</td>
</tr>
<tr>
<td><strong>Zerit®</strong></td>
<td>Stavudine d4T 751</td>
<td>above normal susceptibility range</td>
<td>0.9 1.75</td>
</tr>
<tr>
<td><strong>Ziagen®</strong></td>
<td>Abacavir ABC 676</td>
<td>above normal susceptibility range but below clinical cut-off</td>
<td>1.8 3.0 3.2</td>
</tr>
<tr>
<td><strong>Emtriva™</strong></td>
<td>Emtricitabine FTC 123</td>
<td>above normal susceptibility range</td>
<td>55.0 4.5</td>
</tr>
<tr>
<td><strong>Viread™ (*)</strong></td>
<td>Tenofovir DF TDF 2,883</td>
<td>above normal susceptibility range but below clinical cut-off</td>
<td>0.7 3.0</td>
</tr>
</tbody>
</table>

### NNRTI mutations:
- **None**

<table>
<thead>
<tr>
<th>NNRTI mutations:</th>
<th>Matches in Database</th>
<th>Proportion of Matched Samples</th>
<th>Cut-off Values</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Viramune®</strong></td>
<td>Nevirapine NVP 10,556</td>
<td>within normal susceptibility range</td>
<td>1.3 8.0</td>
</tr>
<tr>
<td><strong>Rescriptor®</strong></td>
<td>Delavirdine DLV 10,342</td>
<td>above normal susceptibility range</td>
<td>1.6 10.0</td>
</tr>
<tr>
<td><strong>Sustiva® / Stocrin®</strong></td>
<td>Efavirenz EFV 12,850</td>
<td>above normal susceptibility range</td>
<td>1.1 6.0</td>
</tr>
</tbody>
</table>

### PI mutations:
- **10I, 20T, 46I, 63P, 71I, 74S, 77I, 90M, 93L**

<table>
<thead>
<tr>
<th>PI mutations:</th>
<th>Matches in Database</th>
<th>Proportion of Matched Samples</th>
<th>Cut-off Values</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Crixivan®</strong></td>
<td>Indinavir IDV 348</td>
<td>above normal susceptibility range</td>
<td>8.9 3.0</td>
</tr>
<tr>
<td><strong>Norvir®</strong></td>
<td>Ritonavir RTV 288</td>
<td>above normal susceptibility range</td>
<td>12.3 3.5</td>
</tr>
<tr>
<td><strong>Viracept®</strong></td>
<td>Nelfinavir NFV 344</td>
<td>above normal susceptibility range</td>
<td>23.6 4.0</td>
</tr>
<tr>
<td><strong>Invirase® / Fortovase®</strong></td>
<td>Saquinavir SQV 899</td>
<td>above normal susceptibility range</td>
<td>3.8 2.5</td>
</tr>
</tbody>
</table>
Analytics: Identify suboptimal ordering and provide feedback

• Given literally thousands of laboratory tests available today, where do we focus our educational efforts?
  - Every hospital has different needs
  - Chart review would identify the problems, but is impractical on a large scale
• Use data mining approach to tease out patterns of inappropriate ordering
ATOP™ (Analyzing Test Ordering Patterns)

- Service offered by ARUP since 1998
- Review test mix for opportunities to:
  - Improve patient care
  - Save money
- “Medical” analysis, not just financial analysis
  - Compare test ordering practices to best available evidence, including national guidelines
Sample of ATOP™ Analytic Methods

• Relative order volumes
  - E.g. HCV PCR vs. HCV RIBA

• Age distribution
  - E.g. urine VMA

• Result distribution
  - E.g. CA-125
• Large academic medical center with active clinical pathology department
• Ordered $50,000/year worth of whole blood drug screens
  - 95% of ARUP’s volume of this panel
• Local pathologists discovered this was due to misunderstanding by transplant services
• Switched to in-house urine drug screens
ATOP™ Case Study #2

- Large academic medical center with active clinical pathology department
- Ordered $20,000/year worth of HCV RIBA confirmations
- Lab manager discovered that this was due to a canned comment applied to HCV screens
  - “If RIBA confirmation is needed, contact the laboratory at…”
Structural Changes ("Rules")

• Requisition forms
  - Paper
  - Online (e.g. CPOE)

• Panels
  - Reject requests for medically questionable panels
  - Create reflex panels where appropriate
Structural Changes ("Rules")

- Diagnostic Utilization Committees
  - Analogous to P&T Committees
  - Set policy related to permissible test orders
- Examples
  - Group Health Cooperative
  - Vanderbilt
Summary

- Overuse, underuse and misuse of diagnostic tests are all common
- Laboratories have numerous tools available for improving utilization
- Reference Laboratories can be a valuable partner to local laboratories in improving utilization