What is an “Inappropriate or Unnecessary” Laboratory Test?

- Any test where results are not likely to be “medically necessary” for appropriate clinical management of the patient

NOT

- Any test where reimbursement is likely to be denied
- How common is inappropriate testing?
  - Prevalence estimated at 25% to 40%
  - Under-testing can be difficult to quantify
  - Huge variability in test request patterns of suggests it is widespread

DISCLOSURES:
Relevant Financial Relationship(s)
- None

Off Label Usage
- None
Some Certainties Related to New Tests

- After a new lab test is released to market, its specificity will decrease over time
  - Galectin-3 and ST2: new serum biomarker assays for use in patients with chronic heart failure (specific utility for a specific clinical condition)
  - Do we want this to be ordered in everyone? NO!

Lab Spending by Discipline

<table>
<thead>
<tr>
<th>Lab Area (by CPT code)</th>
<th>% of Total Spending</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical Pathology</td>
<td>28.3%</td>
</tr>
<tr>
<td>Chemistry</td>
<td>23.5%</td>
</tr>
<tr>
<td>Panels</td>
<td>12.1%</td>
</tr>
<tr>
<td>Microbiology</td>
<td>10.7%</td>
</tr>
<tr>
<td>Immunology</td>
<td>8.0%</td>
</tr>
<tr>
<td>Cytopathology</td>
<td>7.7%</td>
</tr>
<tr>
<td>Hematology</td>
<td>3.1%</td>
</tr>
<tr>
<td>Venipuncture</td>
<td>1.8%</td>
</tr>
<tr>
<td>BRCA1/BRCA2 Testing</td>
<td>1.4%</td>
</tr>
<tr>
<td>Urinalysis</td>
<td>1.3%</td>
</tr>
<tr>
<td>Other</td>
<td>2.7%</td>
</tr>
</tbody>
</table>

Chemistry Tests and Lab Utilization

- Can be almost more difficult because...
  - Often embedded into clinical practice
    - Taught in medical school that...
      - We've always had standing orders for...
      - It's just a... (potassium/ionized calcium/magnesium/blood gases/BNP/glucose/iron)
  - Just a piece of the clinical puzzle (usually not a yes/no answer)
  - Everyone is the expert
Examples of “Waste” and Non-Standard Tests: Chemistry

- Legitimate tests in the wrong clinical setting
  - PSA testing in a 90-year-old man
  - Daily orders for xyz
- Tests without sufficient evidence impacting outcome
  - IgG allergy testing
  - VAP/massive CV risk panels
- Junk science
  - Adrenal stress panel
  - Salivary hormone tests (menopause/aging)
  - Detoxification capacity

Need for Change in Physician Behavior

- Changing behavior is hard
- Education + feedback = most likely to succeed
- Feedback has greatest impact to influence decision-making if it is delivered as close as possible to the time the decision is being made

Control Visibility of the Test

Massachusetts General Study: display test $
Control How the Test is Ordered:
Make it Easy to Order the Right Test Using Computerized Provider Order Entry (CPOE)!

- hCG: useful to diagnose/monitor pregnancy and useful as a tumor marker
  - hCG pregnancy assay:
  - hCG tumor marker assay:

Useful Interpretive Comments for Cardiac Markers: NT-proBNP

- Cardiac biomarker panel
  - Troponin only (CK-MB removed)

Useful Interpretive Comments for Cardiac Markers: Troponin

- Cardiac biomarker panel
  - Troponin only (CK-MB removed)
- Serial samples required, critical to define a “change/delta” in troponin to diagnose AMI
Examples of “Waste” and Non-Standard Tests: Chemistry

Red Cell Folate versus Serum Folate

Folate
- Essential vitamin involved in DNA synthesis
- Deficiency leads to:
  - Neural tube defects (NTD)
  - Neurological manifestations
  - Megaloblastic anemia (MCV >100 fl.)
- Relationship between folate, NTDs, cancer and cardiovascular disease led to mandated FDA fortification of foods (1996-1998)

<table>
<thead>
<tr>
<th>Food</th>
<th>Micrograms (μg)</th>
<th>% DV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breakfast cereals fortified with 100% of DV, 1/2 cup</td>
<td>480</td>
<td>100</td>
</tr>
<tr>
<td>Beef liver, cooked, braised, 3 ounces</td>
<td>195</td>
<td>45</td>
</tr>
<tr>
<td>Spinach, frozen, cooked, boiled, 1/2 cup</td>
<td>100</td>
<td>25</td>
</tr>
<tr>
<td>Legumes, lentils, canned, 1 cup</td>
<td>60</td>
<td>15</td>
</tr>
<tr>
<td>Lettuce, Romaine, shredded, 1/2 cup</td>
<td>40</td>
<td>10</td>
</tr>
<tr>
<td>Wheat germ, whole, 2 tablespoons</td>
<td>40</td>
<td>10</td>
</tr>
<tr>
<td>Orange juice, chilled, includes concentrate, 1/2 cup</td>
<td>35</td>
<td>10</td>
</tr>
</tbody>
</table>

Laboratory Diagnosis of Folate Deficiency
- Complete blood count (CBC)
- Serum folate
  - Immunoassay
  - Recent dietary intake (fasting required)
- Erythrocyte (RBC) folate
  - RBC hemolysate is prepared to release intracellular folate (manual sample prep)
  - Historically regarded as the gold standard for tissue folate deficiency
Ordering Patterns of Serum and RBC Folate:
Is it Necessary to Order Both Tests to Diagnose Folate Deficiency?

<table>
<thead>
<tr>
<th>Test</th>
<th>Mayo Annual Volume</th>
<th>MML Annual Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>Folate (Serum)</td>
<td>12,088</td>
<td>14,223</td>
</tr>
<tr>
<td>Folate (RBC)</td>
<td>2,141</td>
<td>21,678</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Test</th>
<th>Nominal Fee</th>
<th>Medicare Reimbursement</th>
<th>Direct Laboratory Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Folate (Serum)</td>
<td>$120.08</td>
<td>$21.47</td>
<td>$10.11</td>
</tr>
<tr>
<td>Folate (RBC)</td>
<td>$136.46</td>
<td>$25.29</td>
<td>$72.37</td>
</tr>
</tbody>
</table>

Convincing Evidence that RBC Folate Testing is Unwarranted: Modern Folate Deficiency is Rare

- Mayo orders for simultaneous serum and RBC folate assays between 1999-2009 (n=1082)
  - Prevalence of deficiency <0.09% (n = 1, both low)
  - Abnormal defined by NHANES/CDC definition

Serum Folate (ng/mL)
- Deficient (< 3.0)
- Sufficient (> 3.0)

<table>
<thead>
<tr>
<th>RBC Folate (ng/mL)</th>
<th>Deficient (&lt;140)</th>
<th>Sufficient (&gt;140)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 (0.0%)</td>
<td>4 (0.4%)</td>
</tr>
<tr>
<td></td>
<td>8 (0.7%)</td>
<td>1069 (98.8%)</td>
</tr>
</tbody>
</table>

*3 difficult interpretations, 1 emergency department eval/non-fasting
Convincing Evidence that RBC Folate Testing is Unwarranted: Analytical Imprecision

- 2010 CAP Survey
- RBC folate > Serum folate

<table>
<thead>
<tr>
<th>Method</th>
<th># labs</th>
<th>Mean (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Siemens Advia Centaur</td>
<td>427</td>
<td>41.6</td>
</tr>
<tr>
<td>Roche e601/E170</td>
<td>231</td>
<td>3.50</td>
</tr>
<tr>
<td>Beckman Coulter</td>
<td>35</td>
<td>204.2</td>
</tr>
<tr>
<td>Siemens Advia Centaur</td>
<td>317</td>
<td>3.72</td>
</tr>
<tr>
<td>Beckman Coulter</td>
<td>28</td>
<td>122.8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>%CV</th>
<th>Serum Folate</th>
<th>RBC Folate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.50</td>
<td>0.45</td>
</tr>
<tr>
<td>100</td>
<td>41.6</td>
<td>204.2</td>
</tr>
<tr>
<td>200</td>
<td>3.50</td>
<td>3.72</td>
</tr>
<tr>
<td>300</td>
<td>2.72</td>
<td>122.8</td>
</tr>
</tbody>
</table>

Strategies for Obsoleting RBC Folate (or any test)

- Get buy-in from clinicians!
  - Produce institution-specific data showing limited diagnostic utility
- Present data to relevant clinical practice committees
  - Hematology, GI, Endocrinology
- Remove RBC folate test from order sets, “hot buttons” within CPOE, educational material
- Communicate, communicate, communicate
  - Grand Rounds, newsletter, memo, etc.

Folate Testing

- Routine ordering of serum and RBC folate together is unnecessary
- Folic acid supplementation reasonable approach without testing for deficiency
- RBC folate provides equivalent diagnostic information to serum folate in almost all situations
- Laboratories should (with little exception) NOT be ordering RBC folate
Examples of “Waste” and Non-Standard Tests: Chemistry

C-Reactive Protein (CRP) versus
Erythrocyte Sedimentation Rate (ESR)

Acute Phase Reactants: CRP vs. ESR
Acute and chronic inflammation

- CRP
  - Automated
  - TAT ~15 min+
  - Objective measure

- ESR (Westergren method)
  - Manual
  - TAT ~60 min+
  - Subjective measure
  - Prone to technical errors
  - Many false positives (influenced by age, gender, anemia, protein, etc…)

Mayo Clinic Ordering Patterns for ESR and CRP Over 1 Year

~30,000 simultaneous orders!!
Discordance Between ESR and CRP Results

- 900+ unique ICD-9 codes associated with ESR/CRP
- Each test had up to 3 indications for testing
  - 95% of ESR and CRP orders were made for the same indication

<table>
<thead>
<tr>
<th></th>
<th>ESR</th>
<th>Normal</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated CRP</td>
<td>4684</td>
<td>3856</td>
<td>8540</td>
</tr>
<tr>
<td>Normal CRP</td>
<td>1874</td>
<td>19286</td>
<td>21160</td>
</tr>
<tr>
<td>Total CRP</td>
<td>6558</td>
<td>23142</td>
<td>29700</td>
</tr>
</tbody>
</table>

81% Concordance

Clinical Use of ESR and CRP

- Chart review of the "most" discordant panels
- Clinician reaction to the lab result
- CRP clearly the preferred test!

<table>
<thead>
<tr>
<th>Category</th>
<th>% Concordance</th>
<th>Guideline Recommendation</th>
<th>Clinician Reaction to Result/Recommended Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid Arthritis</td>
<td>79</td>
<td>ESR and CRP</td>
<td>Unclear</td>
</tr>
<tr>
<td>Polymyalgia Rheumatica</td>
<td>73</td>
<td>ESR</td>
<td>CRP</td>
</tr>
<tr>
<td>Giant Cell Arteritis</td>
<td>78</td>
<td>ESR</td>
<td>CRP</td>
</tr>
<tr>
<td>Inflammation</td>
<td>83</td>
<td>n/a</td>
<td>CRP</td>
</tr>
</tbody>
</table>

Dealing with the Pseudoscience and Waste

- Often easier than dealing with standard tests (just say no)
- Look for CLIA laboratories that:
  - Claim their tests rule-in syndromes that are not well accepted
  - Dysbiosis, vaccine injury, emotional problems
  - Advertise/claim their tests rule-in syndromes where no specific lab test exists
  - Chronic fatigue, fibromyalgia, autism, irritable bowel syndrome, chemical sensitivity
  - Involve huge panels of testing which may cost $1,000+ (many results of which come back positive)
  - Offer tests which are not referenced in any legitimate peer-reviewed publications
Dealing with the Pseudoscience/Waste and Sendouts

- Structural interventions are good!
  - Formularies are effective
  - Reminders
  - Report cards
  - Authorization in "real time"

Conclusions

- Chemistry tests are highly embedded in clinical practice and may be more difficult to deal with
- Focus on immunoassays (RBC folate) and tests requiring manual handling/special processing (ESR)
- Formularies are effective at eliminating assays/laboratories which are questionable, often expensive and have little-to-no evidence on utility

*Evidence-based medicine should be complemented by evidence-based implementation*

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  - Dr. Jennifer Oliveira
  - Dr. Jim Hoyer

- University of Washington Department of Medicine
  - Dr. Michael Astion, Division Chief of Laboratory Medicine, Seattle Children’s Hospital
What’s next?

- Part 3 in the series
  - Dr. Bobbi Pritt discusses laboratory-driven testing algorithms and test ordering

Questions or requests...
E-mail to: MMLHotTopics@mayo.edu

For more information...
Visit MayoMedicalLaboratories.com
or call Mayo Laboratory Inquiry at 800-533-1710