PITFALLS AND PEARLS: INTERPRETING COMMON LABS IN CLINICAL PRACTICE

FRIDAY/1:30-3:00PM

ACPE UAN: 0107-9999-18-279-L01-P  0.15 CEU/1.5 hr

Activity Type: Application-Based

Learning Objectives for Pharmacists:
Upon completion of this CPE activity participants should be able to:
1. Describe specific pathophysiology associated with common laboratory results.
2. Review normal ranges for common laboratory tests.
3. Identify common causes for abnormal lab values.
4. Interpret clinical significance of abnormal laboratory values.
5. Recognize when to contact prescribers with appropriate recommendations.

Speakers:
Emily Beckett, PharmD, BCPS
Emily Beckett is an Assistant Clinical Professor at the University of Iowa College of Pharmacy and a practicing clinical pharmacist with the Broadlawns Family Medicine Residency Program. She received her Doctor of Pharmacy degree from the University of Iowa College of Pharmacy and completed a PGY1 residency at Mercy Medical Center Des Moines. She assists in the Family Medicine Anticoagulation clinic, as well as provides diabetes education to patients. She assists on-site medical residents with research projects and also precepts University of Iowa pharmacy students. Prior to arriving at Broadlawns Family Health Center, Emily worked at Unity Point – Des Moines providing inpatient anticoagulation, diabetes and heart failure education and precepting Drake University College of Pharmacy students. Her professional interests include anticoagulation, diabetes and chronic disease management, as well as professional education and nutrition. In her free time, she enjoys biking, traveling, and spending time with her husband and three children.
Matthew Cantrell, PharmD, BCPS

Matthew Cantrell is a Clinical Associate Professor in the Department of Pharmacy Practice and Science at the University of Iowa College of Pharmacy and a Clinical Pharmacy Specialist at the Iowa City VA Health Care System. He graduated from Mount Mercy College in 2000 and received his Doctor of Pharmacy degree from the University of Iowa in 2005. He completed a Primary Care Pharmacy Practice Residency at the Iowa City VA in 2006. His primary clinical responsibilities include anticoagulation, primary care, and lipid clinic. He provides didactic and experiential education in the pharmacy curriculum. Additionally, he is a preceptor for the PGY1 pharmacy residency program at the Iowa City VA. Aside from his role as a preceptor for ambulatory care clerkship students, he has served as a preceptor for research & global health rotations focused on underserved populations. Dr. Cantrell is active in many state and national organizations and was previously the Chair of the American College of Clinical Pharmacy Geriatric Practice and Research Network. Dr. Cantrell was named the Teacher of the Year in 2010 and received an award for Faculty Preceptor Excellence in 2011. He was the 2013 recipient of the Distinguished Young Pharmacist Award sponsored by the Iowa Pharmacy Association and Pharmacists’ Mutual Insurance Company.

Speaker Disclosure: Emily Beckett and Matthew Cantrell report no actual or potential conflicts of interest in relation to this CPE activity. Off-label use of medications will not be discussed during this presentation.
Pitfalls and Pearls: Interpreting Common Labs in Clinical Practice

Presented by: Matt Cantrell, PharmD, BCPS
Emily Beckett, PharmD, BCPS
University of Iowa College of Pharmacy

Disclosure

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Learning Objectives

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  - Recognize when to contact prescribers with appropriate recommendations

Subclinical Hypothyroidism

Presented by:
  - Matt Cantrell, PharmD, BCPS
  - University of Iowa College of Pharmacy
  - Iowa City VA Healthcare System
Patient Case

- A 65-year-old woman presents to her provider with a chief complaint of fatigue and weight gain which has attributed to “getting older”
- She has CHF and had a myocardial infarction 2 years ago.
- Laboratory results include normal levels of hemoglobin and creatinine. The thyrotropin (TSH) level is 7.2 mIU per liter with a normal free thyroxine (T4) level of 5.0 mcg/dl.
- What is your recommendation to the provider managing her care?

Subclinical Hypothyroidism

- Biochemical diagnosis
  - Elevated TSH level with a normal T4

- Reference ranges
  - TSH: 0.5-5.0 mU/L
  - Thyroxine 4.6-12 mcg/dl

- 3-15% of the population

- More common in aging women

Symptoms

- Many patients may be asymptomatic especially older patients

- Patients may report
  - Depression symptoms with reduced quality of life
  - Muscle weakness
  - Cold intolerance
  - Fatigue
  - Weight gain
  - Constipation

Potential Long Term Consequences

- Progression to overt hypothyroidism
- Potentially worsening lipid profile
- Loosely associated with elevated BMI and waist circumference
- Potential cardiac risk factor
  - Meta-analysis of 55,000 patients from 11 cohorts

<table>
<thead>
<tr>
<th>Risk of Fatal &amp; non-fatal coronary heart disease events by TSH (mIU/L)</th>
<th>4.5-6.9</th>
<th>7-9.9</th>
<th>10-19.9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hazard Ratio</td>
<td>1.00, (0.86-1.18)</td>
<td>1.17, (0.96-1.43)</td>
<td>1.89, (1.28-2.80)</td>
</tr>
</tbody>
</table>

Other meta-analyses have not established a relationship to fracture risk or cognitive decline

Outcomes Related Research

- 737 patients with subclinical hypothyroidism
- Double-blind, randomized, placebo controlled trial
- 25-50 mcg of levothyroxine vs. placebo

Outcome measures
- Change in Hypothyroid Symptom & Tiredness score on thyroid QOL questionnaire

Results

<table>
<thead>
<tr>
<th>Baseline data</th>
<th>Placebo (N=369)</th>
<th>Levothyroxine (N=368)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>74.8</td>
<td>74.0</td>
</tr>
<tr>
<td>Female Sex</td>
<td>53.7%</td>
<td>53.8%</td>
</tr>
<tr>
<td>Thyrotropin mIU/L</td>
<td>6.38</td>
<td>6.41</td>
</tr>
</tbody>
</table>

- At 12 months:
  - TSH 5.48 mIU/L in placebo vs. 3.63 mIU/L in levothyroxine group
- No difference in Hypothyroid Symptom Scores or the Tiredness Score
- No significant risk of adverse effects with treatment
- Conclusion: No apparent benefit of using levothyroxine for subclinical hypothyroidism
When Treatment is Indicated

- Oral levothyroxine is treatment of choice
- Starting dose is 25-75 mcg
  25 mcg for patients with low weight, angina, or higher risk for CVD
- Further dosing is guided by repeat TSH, generally after 6-8 weeks
- 5% risk of overcorrection
  - When TSH is <0.1 mIU/L may increase risk of atrial fibrillation, osteoporosis, and fractures
Key Points Related to Subclinical Hypothyroidism

• In patients with TSH <7 mIU/L, 50% will normalize within 2 years

• If TSH elevated patients should have TSH and free thyroxine repeated after 2-3 months before treatment initiated to confirm diagnosis

• Treatment is generally recommended for younger patients with TSH levels >10 mIU/L although long term benefits not well established

• Older patients or patients with TSH <10 mIU/L treatment decisions are based on individual patient factors (symptoms, a positive test for antibodies to thyroid peroxidase or cardiac risk factors)

Limitations of A1c as a Marker or Glycemic Control

Presented by:
- Matt Cantrell, PharmD, BCPS
- University of Iowa College of Pharmacy
- Iowa City VA Healthcare System
Patient Case

• **CC:** MD reports for a 1 month follow up appointment to assess treatment for his anemia.

• **HPI:** MD is a 67 year old male with type 2 diabetes (diagnosed 12 months ago with an A1c of 9.2%), CKD and anemia returns for follow up

• **PMH:** Type 2 DM, Hyperlipidemia, Hypertension, CKD and Anemia

• **Current medications:** Metformin 1000 mg BID, Glipizide 10 mg BID, Glargine 15 units at bedtime, Atorvastatin 40 mg daily, Lisinopril 20 mg daily, HCTZ 25 mg daily, Epoetin alpha 50 units/kg 3 times a week

• **Vitals:** Blood pressure: 131/87, Pulse: 75, Respirations: 18

<table>
<thead>
<tr>
<th>Test</th>
<th>Lab Value</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting plasma glucose</td>
<td>167 mg/dL</td>
<td>70-100 mg/dL</td>
</tr>
<tr>
<td>Hba1c</td>
<td>5.5%</td>
<td>4-6%</td>
</tr>
<tr>
<td>White blood cell</td>
<td>6,000 x 10^9/L</td>
<td>4-10 x 10^9/L</td>
</tr>
<tr>
<td>Red blood cell</td>
<td>3.3 M/μl</td>
<td>4.0-6.0 M/μl</td>
</tr>
<tr>
<td>Platelet</td>
<td>500 x 10^9/L</td>
<td>150-450 x 10^9/L</td>
</tr>
<tr>
<td>Hemoglobin*</td>
<td>8.9 g/dL</td>
<td>13.5 to 17.5 g/dL</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>36%</td>
<td>40%-52%</td>
</tr>
<tr>
<td>MCV</td>
<td>70 fl</td>
<td>80-100 fl</td>
</tr>
<tr>
<td>MCHC</td>
<td>28 g/dL</td>
<td>30-35 g/dL</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>2.3 mg/dL</td>
<td>0.8-1.3 mg/dL</td>
</tr>
<tr>
<td>eGFR</td>
<td>15 mL/min/1.73m²</td>
<td>&gt;60mL/min/1.73m²</td>
</tr>
</tbody>
</table>

*hemoglobin measured 4 weeks ago was 7.2 g/dL
History of A1c

- **1978:** A1c considered standard biomarker for glycemic control
- **1988:** American Diabetes Association (ADA) first recommends using A1c
- **1993:** DCCT demonstrated importance as a predictor of diabetes related outcomes
- **1994:** ADA recommends specific A1c targets
- **2010:** ADA added A1c ≥6.5% as diagnostic for diabetes
- **2014:** ACCORD trial - increased risk of death with intense glycemic goal. Results led to individualized goals

What is A1c?

- Formed by attachment (glycation) of hemoglobin and glucose
- Formation occurs slowly over the life span of erythrocyte (~120 days)
- Proportional to average concentration of glucose in erythrocyte during lifespan
  - As more glucose enters blood, more hemoglobin becomes glycated
- Represents a *weighted mean* of glucose levels during the preceding 3 month period
  - Recent acute changes may have greater influence and disproportionately affect A1c (ex: glucocorticoid treatment)
Correlation Between A1c and Estimated Average Glucose

- General rule—every 1% change in A1C is associated with an approximate 30 mg/dL change in estimated average glucose

- Important to recognize discrepancies between average fasting glucose and expected A1c

<table>
<thead>
<tr>
<th>Glucose (mg/dL)</th>
<th>A1c (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>97</td>
<td>5</td>
</tr>
<tr>
<td>126</td>
<td>6</td>
</tr>
<tr>
<td>154</td>
<td>7</td>
</tr>
<tr>
<td>183</td>
<td>8</td>
</tr>
<tr>
<td>212</td>
<td>9</td>
</tr>
<tr>
<td>240</td>
<td>10</td>
</tr>
<tr>
<td>269</td>
<td>11</td>
</tr>
<tr>
<td>298</td>
<td>12</td>
</tr>
</tbody>
</table>
Limitations to Using A1c

• May not adequately predict important clinical endpoints

• A1c can be affected by factors independent of glycemia
  • Clinical and exogenous factors may yield false results

Factors That Alter A1c Accuracy

• Conditions that prolong the life of the erythrocyte or are associated with decreased red cell turnover result in higher A1c levels
  • Iron, vitamin B-12 or folate-deficiency anemias

• Conditions that shorten the life of the erythrocyte or are associated with increased red cell turnover result in lower A1c levels
  • Blood loss, hemolytic anemia, splenomegaly

• Other factors:
  • End-stage renal disease
  • medications & exogenous substances
  • Pregnancy
  • Race
Conditions that Alter A1c Independent of Glycemia

<table>
<thead>
<tr>
<th>Factors Affecting Hb A1c</th>
<th>Falsely Lowered</th>
<th>Falsely Elevated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythrocyte Lifespan</td>
<td>Decreased erythrocyte lifespan: hemolytic anemia, recent blood transfusion; splenomegaly, pregnancy</td>
<td>Increased erythrocyte lifespan: splenectomy</td>
</tr>
<tr>
<td>Erythropoiesis</td>
<td>Reticulocytosis; EPO administration</td>
<td>Iron/Vitamin B12 deficiency</td>
</tr>
<tr>
<td>Assay Interference</td>
<td>Severely elevated triglycerides</td>
<td>Chronic alcohol use</td>
</tr>
<tr>
<td>Glycation</td>
<td>High dose vitamin C or E</td>
<td>CKD</td>
</tr>
</tbody>
</table>

Erythrocyte Stimulating Agents (ESA) Effect on A1c

Effect of Ethnicity on A1c

- Numerous studies have noted racial and ethnic differences in A1c but have often simply attributed these differences due to differences to access to care or quality of care.

- Even after adjusting for potential confounders, A1c levels were significantly higher in Black, Hispanic, American Indian, and Asians compared to Whites.
  - DURABLE Trial showed mean A1c levels were 0.37% higher in Blacks, 0.27% higher in Hispanics, 0.33% higher in Asians compared to Whites.

- To date it has not been studied if there are racial/ethnic differences in RBC survival or genetic determinants of hemoglobin glycation.

- Further research is needed to determine if these racial differences in A1c also modify risk of diabetes related complications.


Alternatives to A1c: Fructosamine

- What is it?
  - Refers to glycation of protein (usually albumin) to sugar.
  - Reflects shorter period of glycemic control compared to A1C.
    - Lifespan of albumin ~20 days vs 120 days for erythrocyte.

- Uses
  - When A1c may be inaccurate.
  - Provides better assessment of more recent changes in glycemic control.
  - End stage renal disease (A1c underestimates glycemic control).

- Limitations
  - Dependent on albumin concentrations.
    - Hypoproteinemia/hypoalbuminemia may falsely lower.
    - Unclear if corrections for this are necessary.

<table>
<thead>
<tr>
<th>Glucose (mg/dl)</th>
<th>Fructosamine (umol)</th>
<th>HbA₁c (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>90</td>
<td>212.5</td>
<td>5.0</td>
</tr>
<tr>
<td>120</td>
<td>250</td>
<td>6.0</td>
</tr>
<tr>
<td>150</td>
<td>287.5</td>
<td>7.0</td>
</tr>
<tr>
<td>180</td>
<td>325</td>
<td>8.0</td>
</tr>
<tr>
<td>210</td>
<td>362.5</td>
<td>9.0</td>
</tr>
<tr>
<td>240</td>
<td>400</td>
<td>10.0</td>
</tr>
<tr>
<td>270</td>
<td>437.5</td>
<td>11.0</td>
</tr>
<tr>
<td>300</td>
<td>475</td>
<td>12.0</td>
</tr>
<tr>
<td>330</td>
<td>512.5</td>
<td>13.0</td>
</tr>
<tr>
<td>360</td>
<td>550</td>
<td>14.0</td>
</tr>
<tr>
<td>390</td>
<td>587.5</td>
<td>15.0</td>
</tr>
</tbody>
</table>

**Patient Case**

- MD is responsive to treatment with Epoetin alpha. Continue treatment to manage anemia

- Based on A1c of 5.5%, MD is experiencing good glycemic control. However, based on fasting plasma glucose level he is not well controlled on his current diabetic regimen

- Plan: Order fructosamine to better assess glycemic control
Hyperuricemia

Presented by:
- Matt Cantrell, PharmD, BCPS
- University of Iowa College of Pharmacy
- Iowa City VA Healthcare System

Patient Case

An 80-year-old man presents to the clinic for an annual checkup. He has no chief complaints and denies prior or current gout symptoms.

His medical history is notable for hyperlipidemia, hypertriglyceridemia, and hypertension. He has an intolerance to statin therapy.

Laboratory values are as follows: serum urate 9.2 mg/dL, SCr 1.6 mg/dL, WBC 10.0 × 10^3 cells, Hgb 13.8 mg/dL, LDL 62 mg/dL, and HDL 46 mg/dL. His blood pressure is 124/68 mm Hg.

His home medications include HCTZ, niacin, and amlodipine.

What would you recommend for this patient?
Hyperuricemia vs. Gout

- Hyperuricemia
  - No universally accepted definition
  - Generally Serum urate concentration >6.8 mg/dl
  - Often asymptomatic
  - Either overproduction or underexcretion of UA

- Gout
  - Most common inflammatory arthritis
  - Hyperuricemia with crystal deposition
  - Upon diagnosis target UA <6 mg/dL and <5 mg/dl in patients with tophaceous gout

Uric Acid vs. Gout

- Crystals can form in vitro above a urate level of 6.8 mg/dl
  - Not all individuals will have crystal deposits at this threshold
- Only 10-20% with hyperuricemia develop gout over 5 years

Should isolated hyperuricemia be medically managed?
Initial Evaluation

• History and Physical Examination

• Medication use

• Lifestyle factors

• Family and Social History

• Laboratory Values
  •CBC, electrolytes, UA, liver function tests, calcium

Lifestyle Factors

• Red meat
• Organ meat
• Seafood with high purine content
• Alcohol
• High fructose corn syrup
Medications that May Cause Hyperuricemia

- Aspirin
- Cyclosporine
- Cytotoxic chemotherapy
- Diuretics
- Niacin
- Teriparatide
- Testosterone

Reasons to consider treatment

- Prevent progression to overt gout
- Hyperuricemia associated with CKD
- Prevent nephrolithiasis
Emerging Reasons for Future Research

- Renewed interest in managing hyperuricemia based on associated co-morbidities
- Prospective observational studies have shown that elevate UA associated with HTN, CV disease, renal disease

<table>
<thead>
<tr>
<th>Condition</th>
<th>Relative Risk</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>1.48</td>
<td>1.33-1.65</td>
</tr>
<tr>
<td>Coronary Heart Disease</td>
<td>1.34</td>
<td>1.19-1.49</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.41</td>
<td>1.05-1.30</td>
</tr>
<tr>
<td>Renal Disease</td>
<td>2.35</td>
<td>1.59-3.46</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>1.24</td>
<td>1.09-1.42</td>
</tr>
</tbody>
</table>

Situations That Might Favor Treatment

- Sustained marked hyperuricemia
- Individuals with uricosuria
- Individuals at risk for tumor lysis syndrome
Reasons to Avoid Treatment of Asymptomatic Hyperuricemia

• Most patients will **NOT** progress to gout

• Added treatment costs

• Lack of data demonstrating benefit

• Treatment may have long term risks

What’s the risk?

• Allopurinol hypersensitivity syndrome
  • 1/1000 patients
  • SJS, TEN and DRESS
  • Mortality up to 25%

• HLA-B*5801 allele strongly associated with hypersensitivity
  • Most prevalent in Chinese, Korean, Thai populations
  • Consider testing prior to initiation especially in these populations

• Febuxostat
  • Higher rates of CV & thromboembolic events
  • Acute hepatic impairment
  • Serious skin reactions
Back to our case

An 80-year-old man presents to the clinic for an annual checkup. He has no chief complaints and denies prior or current gout symptoms. His medical history is notable for hyperlipidemia and hypertension. He has an intolerance to statin therapy. Laboratory values are as follows: serum urate 7.2 mg/dL, SCr 1.6 mg/dL, WBC 10.0 × 10^3 cells, Hgb 13.8 mg/dL, LDL 62 mg/dL, and HDL 46 mg/dL. His blood pressure is 124/68 mm Hg. His home drugs include HCTZ, niacin and amlodipine.

Which one of the following is best to recommend for this patient?

• Both fenofibrate and losartan have demonstrated uricosuric effects and substitution of one or both may be reasonable alternatives in this patient.
Patient case

A 50-year-old male with uncontrolled type 2 diabetes mellitus presents to the emergency room with chief complaint of chest pain and is admitted onto your service. With initial labs, the physician also orders a urinalysis. Patient reports urgency and frequency but denies any flank pain or incontinence. Laboratory results are as follows:

- Appearance = hazy
- pH = 6.0
- Nitrite = positive
- Leukocyte esterase = 2+
- RBC = occasional
- WBC = 20 – 30
- Epithelial cells = 1-5 squamous
- Bacteria = 4+

What is your recommendation to the provider managing his case?
Urinalysis

- Valuable diagnostic test for many common disease states
- Urinary Tract Infection (UTI) is the second most common diagnosed infection in both inpatient and outpatient populations
- Misinterpretation may lead to overtreatment of UTI and increased use of antibiotics

Urinalysis Example

<table>
<thead>
<tr>
<th>URINALYSIS MICROSCOPIC IF INDICATED</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>COLOR YELLOW</td>
<td></td>
</tr>
<tr>
<td>APPEARANCE HAZY</td>
<td></td>
</tr>
<tr>
<td>GLUCOSE NEGATIVE</td>
<td></td>
</tr>
<tr>
<td>BILIRUBIN NEGATIVE</td>
<td></td>
</tr>
<tr>
<td>KETONE NEGATIVE</td>
<td></td>
</tr>
<tr>
<td>SPEC GRAY 1.007</td>
<td></td>
</tr>
<tr>
<td>BLOOD NEGATIVE</td>
<td></td>
</tr>
<tr>
<td>pH 6.0</td>
<td></td>
</tr>
<tr>
<td>PROTEIN NEGATIVE</td>
<td></td>
</tr>
<tr>
<td>UROBILINURIN 0.3</td>
<td></td>
</tr>
<tr>
<td>NITRITE POSITIVE</td>
<td></td>
</tr>
<tr>
<td>LEUK ESTERASE 2+</td>
<td></td>
</tr>
<tr>
<td>MICROSCOPIC INDICATED? YES</td>
<td></td>
</tr>
</tbody>
</table>

| URINE MICROSCOPIC                  |  |
| RBC OCASSIONAL H                  |  |
| WBC 20 – 30 H                     |  |
| EPITHELIAL CELLS 1 – 5 SQUAMOUS H |  |
| BACTERIA 4+ H                     |  |
| IS A URINE CULTURE INDICATED? YES |  |

*Values outside the reference range should be interpreted in context with the patient's clinical condition.*
Urinalysis Example

<table>
<thead>
<tr>
<th>URINALYSIS MICROSCOPIC IF INDICATED</th>
<th>YES</th>
<th>NEGATIVE</th>
</tr>
</thead>
<tbody>
<tr>
<td>COLOR</td>
<td>YELLOW</td>
<td>YELLOW</td>
</tr>
<tr>
<td>APPEARANCE</td>
<td>HAZY</td>
<td>CLEAR</td>
</tr>
<tr>
<td>GLUCOSE</td>
<td>NEGATIVE</td>
<td>NEGATIVE</td>
</tr>
<tr>
<td>BILIRUBIN</td>
<td>NEGATIVE</td>
<td>NEGATIVE</td>
</tr>
<tr>
<td>KETONE</td>
<td>NEGATIVE</td>
<td>NEGATIVE</td>
</tr>
<tr>
<td>SPEC GRAV</td>
<td>1.017</td>
<td>1.010 – 1.035</td>
</tr>
<tr>
<td>BLOOD</td>
<td>NEGATIVE</td>
<td>TRACE</td>
</tr>
<tr>
<td>PH</td>
<td>6.0</td>
<td>5.5 – 8.0</td>
</tr>
<tr>
<td>PROTEIN</td>
<td>NEGATIVE</td>
<td>NEGATIVE</td>
</tr>
<tr>
<td>LEUKESTERASE</td>
<td>POSITIVE</td>
<td>NEGATIVE</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>URINE MICROSCOPIC</th>
<th>YES</th>
<th>NEGATIVE</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBC</td>
<td>OCCASIONAL</td>
<td>NONE SEEN</td>
</tr>
<tr>
<td>WBC</td>
<td>15</td>
<td>NONE SEEN</td>
</tr>
<tr>
<td>LEUKOCYTES</td>
<td>1 – 5 MILLIONS</td>
<td>20 – 30</td>
</tr>
<tr>
<td>BACTERIA</td>
<td>0 – 10</td>
<td>0 – 10</td>
</tr>
</tbody>
</table>

Indicates presence of inflammation
Low specificity and positive predictive value
Negative predictive value ~90%
False positives include:
- Chronic interstitial nephritis
- Uroepithelial tumors
- Infection with atypical organism

Lab Values

- **Urine WBC**: pyuria
  - Normal = WBC < 5
  - Abnormal = WBC > 10

- **Leukocyte esterase**: pyuria
  - Normal = negative
  - Abnormal = positive

---

Lab Values

- **Bacteria**
  - Normal = negative
  - Abnormal = 5+ (~100,000 colony-forming units (CFUs)/mL)
    - 2+ (considered positive for UTI in catheterized or strongly symptomatic patients)
    - Lower amounts may be seen in men, if already on treatment, and if non-E Coli/Proteus organism
  - Any amount of bacteria in the urine may suggest UTI in symptomatic patient

- **Nitrite**
  - Normal = negative
  - Abnormal = positive
    - Indicates presence of organism that reduces nitrate
    - Highly specific for bacterial infection
  - Not all pathogens in the urine are nitrate reducers!
    - Low sensitivity: Negative test does NOT exclude infection
    - Low pH and urine <4hr old may confer false negatives
    - False-positive possibility when dipstick exposed to air or if patient using phenazopyridine

---

**Lab Value Summary**

<table>
<thead>
<tr>
<th>Test</th>
<th>Usual Range</th>
<th>Indicators of Infection</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>&lt; 5</td>
<td>WBC &gt; 10 = pyuria</td>
<td>High sensitivity</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Low specificity</td>
</tr>
<tr>
<td>Leukocyte</td>
<td>Absent</td>
<td>Positive = pyuria</td>
<td>High sensitivity</td>
</tr>
<tr>
<td>Esterase</td>
<td></td>
<td></td>
<td>Low specificity</td>
</tr>
<tr>
<td>Bacteria</td>
<td>Absent</td>
<td>Any amount (5+)</td>
<td>Low sensitivity</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High specificity</td>
</tr>
<tr>
<td>Nitrite</td>
<td>Absent</td>
<td>Positive = presence of bacteria that reduce nitrate</td>
<td>Low sensitivity</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High specificity</td>
</tr>
</tbody>
</table>
Asymptomatic vs Symptomatic

**Asymptomatic Bacteriuria**
- Prevalence increases with age
- Reported in ~50% of women in long-term care facilities
- Routine screening is NOT recommended according to Infectious Diseases Society of America Guidelines
- Pregnant women and patients with a planned transurethral resection of prostate (or procedure where mucosal bleeding is expected) have shown benefit from subsequent culture screening

**Symptomatic Bacteriuria**
- After diagnosis of UTI with urinalysis and symptoms:
  - Empirical antibiotic therapy until culture results are obtained

Clinical Presentation

**Cystitis/Lower UTI Symptoms**
- Dysuria or acute pain
- Frequent urination
- Urgency
- Incontinence
- Occasionally: hematuria, cloudy or foul-smelling urine may be present

**Pyelonephritis/Upper UTI Symptoms**
- Usually has more severe, systemic symptoms
- Urinary symptoms described with cystitis AND
  - Suprapubic pain
  - Flank pain
  - Fever
  - Chills
  - Elevated WBC
  - Nausea and vomiting
Clinical Presentation

- **Uncomplicated UTI**
  - UTI without structural or urologic abnormalities
  - Usually healthy women

- **Complicated UTI**
  - Usually males (due to longer urethra)
  - Presence of foreign body
  - Obstruction
  - Immunosuppression
  - Poorly controlled diabetes mellitus
  - Renal failure or transplantation
  - Urinary retention
  - Pregnancy

When Treatment is Indicated

- Treatment of an UTI **should not be initiated** based on urinalysis alone
  - Patient history, urinary symptoms and urine culture are important for the diagnosis of an UTI
- If asymptomatic bacteriuria is identified in pregnancy, urologic procedures or women with bacteriuria >48h after catheter removal – treatment is warranted
- Empiric antibiotic selection should consider most likely bacteria
  - Uncomplicated: E coli, P mirabilis, K pneumoniae & S saprophyticus
  - Complicated: same as above
    - More resistance seen with gram-negative pathogens
Key Points

- Interpretation of urinalysis requires the understanding of each lab test as well as the incorporation of the patients urinary symptoms

- Pharmacists play a key role in analyzing positive urinalysis and urine cultures in regards to antimicrobial stewardship

- In order to prevent asymptomatic UTI overtreatment, it is important to assess patients symptoms

Back to Our Case

- A 50-year-old male with uncontrolled type 2 diabetes mellitus presents to the emergency room with chief complaint of chest pain and is admitted onto your service. With initial labs, the physician also orders a urinalysis. Patient reports urgency and frequency but denies any flank pain or incontinence. Laboratory results are as follows:
  - Appearance = hazy
  - pH = 6.0
  - Nitrite = positive
  - Leukocyte Esterase = 2+
  - RBC = occasional
  - WBC = 20 – 30
  - Epithelial cells = 1-5 squamous
  - Bacteria = 4+

- Would you recommend obtaining a urine culture?
- Would you begin empiric antimicrobial therapy?
Patient Case

• A 55 year old male with diabetes and hypertension presents to the clinic with a 6 month history of decreased energy, weight gain, and erectile dysfunction. A total testosterone level was taken this morning and came back at 281 ng/dL (ref. range 300-900 ng/dL)

• How do you interpret these results?
• What is your recommendation to the provider for managing his care?
Testosterone

- 98% of circulating testosterone is protein bound
  - About half bound to albumin
  - About half bound to sex hormone-binding globulin (SHBG)
- Only about 0.5-3% of testosterone is in the "free" readily usable form
- Levels of testosterone peak in the morning hours (7-11 AM) and gradually decline throughout the day
- Average decline of serum total testosterone is about 1-2% per year starting at about 40 years old

Buttani, et al. Primary Care Reports. 23(1) Jan 2017.
Lab Tests

• **Serum total testosterone (TT)**
  - References ranges vary by laboratory assays
  - Manifestations typically become evident at lower end of normal, <300 ng/mL for most labs
  - Certain disorders can affect SHBG, which can alter the TT level
    - Falsely elevates TT: aging, hepatic cirrhosis, hepatitis, hyperthyroidism, use of estrogens, HIV or AIDS
    - Falsely decrease TT: obesity, hypothyroidism, diabetes, chronic administration of glucocorticoids, progestins, and testosterone

• **Serum free testosterone**
  - Reference ranges also very by laboratory assays
  - Likely to be a more reliable test when compared to total testosterone
  - May be used if suspect alterations in SHBG

Butanis, et al. Primary Care Reports. 23(1) Jan 2017.

Lab Tests

• Routine screening is **not** recommended in patients who are asymptomatic
• Testing should be performed within the peak morning hours when levels are highest
• A single low testosterone value should always be confirmed by a second measurement on a different day
  - Up to 30% of patients with initial low measurement return as within normal limits upon recheck

Butanis, et al. Primary Care Reports. 23(1) Jan 2017.
Secondary Lab Tests

- Luteinizing Hormone (LH)
- Follicle Stimulating Hormone (FSH)
  - May help determine primary vs. secondary diagnosis
  - May see these levels but often with a referral to endocrinology
- Elevated levels indicate primary hypogonadism
- Low or inappropriately normal levels indicate secondary hypogonadism
- Age-related hypogonadism
  - Decreases in both testicular and hypothalamic-pituitary function

Butanis, et al. Primary Care Reports. 23(1) Jan 2017.

Acquired Causes of Hypogonadism

- **Primary**
  - Infections
  - Type 1 Diabetes
  - Testicular trauma
  - Chemotherapy
  - Alcohol
  - Marijuana
  - Radiation
  - Pesticides
  - Amyloidosis
  - Hyperthyroidism
  - Hepatic cirrhosis

- **Secondary**
  - Obesity
  - Eating disorders
  - Type 2 Diabetes
  - Obstructive sleep apnea
  - Hyperprolactinemia
  - Opioids, steroids
  - Alcohol
  - Acute illness
  - Chronic diseases
  - Hypothyroidism
  - HIV

Butanis, et al. Primary Care Reports. 23(1) Jan 2017.
Clinical Presentation

- **Specific**
  - Decrease libido
  - Decreased spontaneous erections
  - Gynecomastia
  - Loss of body hair
  - Testicular atrophy
  - Infertility
  - Hot flashes

- **Nonspecific**
  - Decreased energy
  - Decreased motivation
  - Depressed mood
  - Sleepiness
  - Reduced muscle
  - Increased body fat
  - Increased BMI
  - Diminished physical performance

Risks of Testosterone Replacement Therapy (TRT)

- Possible increased cardiovascular risk
  - MI and ischemic stroke

- Adverse outcomes
  - Increase hematocrit, prostate specific antigen, blood sugars
  - Adverse lipid pattern
  - Fluid retention
  - Worsening sleep apnea

- Treatment contraindicated in:
  - Active prostate or breast cancer
  - Patient desiring fertility
  - Uncontrolled heart failure
  - Hematocrit >55%
When Treatment is Indicated

- Cause of hypogonadism should be sought before TRT is initiated
- TRT documented to have several clinical benefits including improvements in libido, erectile function, and muscle mass
- Many formulations available
  - Transdermal
  - Intramuscular
  - Intranasal
  - Buccal
  - Intradermal Pellets

Key Points

- Testosterone levels should be drawn in the morning and low levels should be confirmed by second draw on a different day
- Serum total testosterone can be affected due to changes in sex hormone-binding globulin (SHBG)
  - Serum free testosterone is generally more reliable
- Testosterone replacement therapy (TRT) has risks which should be considered along with lab values and symptoms before initiating therapy
Back to Our Case

• A 55 year old male with diabetes and hypertension presents to the clinic with a 6 month history of decreased energy, weight gain, and erectile dysfunction. A total testosterone level was taken this morning and came back at 281 ng/dL (ref. range 300-900 ng/dL).

• How do you interpret these results?
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Anemia

Presented by:
• Emily Beckett, PharmD, BCPS
• University of Iowa College of Pharmacy
• Broadlawns Family Health Center Residency
Patient Case

• A 54 year old female patient presents to your pharmacy with the following lab results and wants to know if she should take some OTC iron to feel less fatigued. How do you respond?

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<tr>
<th>Lab</th>
<th>Patient Results</th>
<th>Relative Value</th>
<th>Normal</th>
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</table>

Anemia

• Defined as reduced number of circulating red blood cells (RBC)
  • Low hemoglobin (Hgb), hematocrit (Hct) or RBC count
    • Definition varies; exercise, altitude, smoking, race, etc can alter Hgb ‘normal’
    • Men: Hgb <13.5 g/dL or Hct <41%  
    • Women: Hgb <12 g/dL or Hct <36%

• Consequences
  • Decreased oxygen delivery
    • Leg cramps, impaired cardiac compensation, respiratory dysfunction
  • Hypovolemia
    • Syncope, dizziness, hypotension, tachycardia, shock

• Signs and symptoms
  • Fatigue, pallor, palpitations, muscle cramps, headache, shortness of breath, confusion
Anemia Causes

- Decreased red cell production
  - Lack of nutrients (B12, iron, folate)
  - Bone marrow disorders
  - Low erythropoietin
- Increased red cell destruction
  - Hemolytic anemias
  - Hypersplenism
- Blood loss – MOST COMMON
  - Obvious bleeding (trauma, hematemesis, melena, menorrhagia)
  - Occult bleeding (slow bleeding ulcer or carcinoma)
  - Induced bleeding (repeated lab tests, hemodialysis losses, excessive blood donation)

Medication Causes of Anemia

- Decrease iron absorption
  - Al-, Mg-, and Ca containing antacids
  - Tetracycline, doxycycline
  - H2RAs
  - PPIs
  - Cholestyramine
- Hemolytic anemia
  - Cephalosporins
  - Levodopa
  - Methylpapava
  - Nitrofurantoin
  - NSAIDs
  - Phenazopyridine
- Blood loss
  - ASA, NSAIDs
  - Anticoagulants
  - Glucocorticoids
- Reduced B12/folate
  - Chemotherapy
  - Hydroxyurea
  - Zidovudine
  - Methotrexate
  - Azathioprine
  - Metformin
  - Folate antagonists
    - Methotrexate
    - Trimethoprim
    - Triamterene
Red Cell Indices

- MCV – mean corpuscular volume
  - Average size of RBC
- MCH – mean corpuscular hemoglobin
  - Average Hgb content in a RBC
- MCHC – mean corpuscular hemoglobin concentration
  - Average Hgb concentration per volume RBC
- Reticulocyte count
  - RBCs live for ~100 days; 1% RBCs replaced with young RBCs daily
  - High = erythropoietic response = marrow is working
  - Low = bone marrow suppression

Am Fam Physician. 2010;82(9):1117–1122

75
Issues with Red Cell Indices

- Hgb, Hct and RBC = concentrations
- Dependent on red cell mass and plasma volume
  - Acute bleeding – may have normal Hgb/Hct until 36-48hr later
  - Pregnancy – Expanded plasma volume = “dilutional” anemia
  - Volume depletion – Less plasma volume may mask anemia

Evaluation of the Patient

- Is the patient bleeding? Now or in the past?
  - Tarry stools, blood in urine? Menstrual flow?
- Is the white count low?
  - Bone marrow suppression, hypersplenism, or aplastic anemia?
- Medication history?
- Change in diet? Weight loss?
  - Low in iron, B12 or folate? Increase in alcohol? Up-to-date on cancer screening?
- History of anemia? New or worsening?
  - Chronic inflammatory disease? Chronic kidney disease?
Iron Studies

• Serum Iron
  • Measures circulating iron; may be influenced by dietary iron – draw after overnight fast

• Total iron binding capacity (TIBC)
  • Circulating transport protein for iron
  • Increased when iron is low

• Total iron saturation (TSAT)
  • Serum iron divided by TIBC x 100
  • Low in iron-deficiency anemia

• Ferritin
  • Iron storage protein – low in iron-deficiency anemia
  • Also acute phase reactant – increases in response to inflammation; may mask low iron stores

Other Lab Tests in Anemia

• Macrocytic anemia
  • B12
    • Deficiency may exist prior to recognition of low levels
    • Serum values are maintained at the expense of vitamin B12 tissue stores
    • Also low due to folate deficiency and pregnancy
  • Folate
    • Serum levels affected by drug-induced folic acid deficiencies and diet/alcohol intake
    • Erythrocyte folic acid levels may be more reliable
Pharmacist Role and Key Points

- Refer patients to ensure correct diagnosis!
  - Verify communication with providers
  - Avoid treatment based on labs without full work-up
    - Example: thalassemias – OTC iron can lead to iron overload
- Identify medication causes for anemia
  - Contact prescribers with causes and alternative solutions
- Assist with therapy recommendations
  - OTC medications, diet recommendations, iron administration counseling
  - Ensure patient has follow-up with provider
- Make sure to include all members of pharmacy in follow-through process
Patient Case

- A 54 year old female patient presents to your pharmacy with the following lab results and wants to know if she should take some OTC iron to feel less fatigued. How do you respond?
- Of note, she just tells you she has recent knee pain and started taking ‘lots of Advil’ and a ‘OTC ulcer medicine’ and her stools are black…

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Take Home Points

- Understand specific pathophysiology associated with common laboratory results
- Identify abnormal values for common laboratory tests and interpret clinical significance of abnormal laboratory values
- Recognize when to contact prescribers with appropriate recommendations
Questions?

Presented by: Matt Cantrell, PharmD, BCPS
Emily Beckett, PharmD, BCPS
University of Iowa College of Pharmacy

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