This Path-O-Gram (POG) begins with an overview of our pathology department as illustrated by the organizational chart. Dr. Attilio Orazi, the pathology department chief, leads anatomic and clinical pathology responsibilities, efforts, and goals shared by our strong team of pathologists, scientists, managers, and technical experts in the field of laboratory medicine. This and subsequent POG newsletters will communicate short and long-term departmental goals as well as recent successes.

With respect to longer term goals, we are planning and developing logistics to implement our pathology residency program with a projected start of July 2023. Dr. Nawar Hakim is in the lead as Program Director.

Recent successes include selection of Dr. Attilio Orazi as the only pathologist in El Paso to make the list for both Pathology and Hematology specialties (https://www.super-doctors.com/texas/El-Paso/Pathology/browse). Additionally, Dr. Orazi’s publication on myeloid neoplasms was featured in The Pathologist (DEC 2020; pp.12-26).
II. Anatomic Pathology

Coccidioidomycosis in a patient with undiagnosed HIV-1
Dr. Angelica Padilla

Autopsy Case Report:
67-year old Hispanic female from New Mexico with no past medical history or recent travel history presented to the emergency department (ED) with:

- a one month history of vague abdominal pain
- 20-pound weight loss in 1 month
- generalized weakness with malaise
- dry cough with occasional clear sputum
- nausea
- non-bloody diarrhea
- arthralgia
- COVID-19 negative

She denies any fevers, chills, or rash. The decedent had visited a private local physician a few days prior and was prescribed oral ciprofloxacin and metronidazole. No diagnostic tests were performed.

In the ED, the decedent presented with:

- respiratory failure
- acute renal failure
- septic shock
- Anemia and low hematocrit
- Liver enzymes were 2X upper limit of normal
- blood pressure was 84/61 mmHg
- pulse rate 128/minute
- respiratory rate 27/minute with pulse oximetry 92% on ambient air

Lymphadenopathy in the cervical area, supraclavicular area, inguinal and axillary regions was palpated.

Admission testing revealed a previously undiagnosed HIV-1 result (viral load 402,000; CD4 = 30). A chest film on admission showed a diffuse micronodular pattern. A CT scan of the chest without contrast revealed extensive diffuse bilateral micronodules in a miliary pattern and mediastinal/axillary lymphadenopathy (up to 3 cm). A CT scan of the abdomen and pelvis revealed enlarged lymph nodes in the para-aortic, gastrohepatic, inguinal, external and internal iliac chains.

The patient died on hospital day 2 despite aggressive treatment with vasopressors, mechanical ventilation, and continuous renal replacement therapy.

Autopsy findings
An autopsy restricted to lungs and lymph nodes was performed. There were bilateral pleural lung effusions (approximately 400 cc on the right side and 300 cc on the left side). The lungs were grossly boggy and congested, the right lung weighed 1400 g (mean 450 g) and the left lung weighed 1250 g (mean 400 g). There were bilateral innumerable diffuse tan nodules with miliary spread in the upper and lower lung lobes with predominance in the upper lobes [Figs E]. Microscopically, the lungs had intra-alveolar edema, alveolar collapse, capillary congestion, and histiocytes. Additionally, there is caseating granulomatous inflammation with abundant coccidioides spherules with and without endospores that can be seen in H&E and GMS stains [Figs C & D]. Of note, an acid-fast bacilli stain was negative.

The decedent grossly had extensive cervical, supraclavicular, inguinal, and axillary lymphadenopathy. The lymph nodes were enlarged and had a cut white/tan surface [Fig F]. Microscopically, the normal lymph node architecture was replaced with granulomatous inflammation showing Coccidioides on Hematoxylin and eosin stain (H&E) and special fungal stain Grocott-Gomori’s methenamine silver stain (GMS) [Figs A & B].

Fig A. Normal lymph node architecture is replaced with granulomatous inflammation with Coccidioides fungal organisms (H&E 20X).

Fig B. Lymph node Grocott-Gomori’s methenamine silver stain (GMS) highlights Coccidioides fungal organisms (20X). Note empty spherules and spherules filled with endospores.
Coccidioidomycosis

Coccidioidomycosis is a fungal infection caused by inhalation of spores from *Coccidioides immitis* or *Coccidioides posadasii*. It is typically found in the soil in the southwestern United States, Mexico, Central America, and South America. Outbreaks have been linked to earthquakes, windstorms, and military training exercises where the ground is disturbed. Infections are usually self-limited: 60% of patients are asymptomatic or have mild respiratory illnesses, and 1% will develop disseminated Coccidioidomycosis regardless of their immune status. Risk factors for dissemination include HIV infection, pregnancy, and immunosuppression. There may be a genetic predisposition because certain ethnic populations are more susceptible to disseminated disease. The risk of dissemination is 175 times greater in Filipinos and 10 times greater in African Americans than non-Hispanic whites.

Patients with coccidioidal infection develop symptoms of their acute illness 7 to 21 days after exposure. Clinical symptoms are non-specific and can overlap with other infections or medical conditions. The fungus infects the lungs and can disseminate hematogenously to other body locations.

**Diagnosis: Coccidioidomycosis**

Several routine laboratory tests although non-specific may be abnormal including:
- Increased peripheral white blood cell count
- Eosinophilia
- Elevated erythrocyte sedimentation rate
- Elevated (1,3)-beta-D-glucan in blood or CSF

**Tests used to detect Coccidioidomycosis:**
- Serologic tests for antibodies including enzyme-linked immunoadsorbent assays (ELISA), immunodiffusion tests, complement fixation assay, and tube precipitin-type antibodies
- Antigen in urine, blood, CSF, body fluids
- Culture
- Microscopic ID in clinical specimens
- Polymerase chain reaction

Serologic tests for antibodies is the most common approach; however, detectable antibodies may not have formed early in infection or in immunocompromised patients, especially those without extensive disease.

**Clinical pearls:**
- Coccidioidomycosis is a fungal infection caused by inhalation of spores from *Coccidioides immitis* or *Coccidioides posadasii*, usually found in the soil in the southwestern United States.
- Risk factors include HIV infection, pregnancy, and immunosuppression.
- Infections are usually self-limited.
- Serologic tests for antibodies is the most common diagnostic approach.
- Antigen detection, culture, and microscopic identification may be helpful in immunocompromised patients with extensive disease.

**Summary**
The decedent presented in acute septic shock with multi-organ failure secondary to disseminated infection with *Coccidioides* infection. She had a newly diagnosed
HIV/AIDS with clinical findings that were non-specific for a particular infectious entity. Clinically lymphoma, tuberculosis, and infections with other microorganisms were suspected. However, the decedent died within a couple of days from admission before a complete workup was performed. Due to the COVID-19 pandemic and the clinical overlap with other infections, Coccidioidomycosis may get misdiagnosed.

Due to the COVID-19 pandemic and the clinical overlap with other infections, Coccidioidomycosis may get misdiagnosed.

For more info contact Dr. Angelica Padilla: 915 996-4956

III A. Clinical Pathology: Microbiology

Current state of SARS-CoV-2 testing at UMC
Dr. Aaron Geno

Polymerase chain reaction and other nucleic acid amplification methods are adaptable technologies with a proven track record in diagnosing infectious diseases. The adaptability of these technologies allowed many different assays to be rapidly developed for detecting SARS-CoV-2, the causative agent of the COVID-19 pandemic. Let’s look at some of the technologies in use at UMC.

Real Time RT-PCR
- Reverse transcriptase PCR converts RNA to DNA
- DNA is amplified through sequential cycling
  o DNA denatured with heat ("melting")
  o Short pieces of DNA bind to their targets ("annealing")
  o Polymerases extend primers to copy DNA ("elongation")
- Use of labeled probes or intercalating dyes permits monitoring of the reaction in real time
- Luminescent threshold discriminates positive from negative
- Cycle at which the reaction crosses this threshold known as threshold cycle (Ct)
- Can be made quantitative through use of standard curves (absolute quantitation) or internal controls (relative quantitation)

Isothermal Amplification
- Many variations available through clever exploitation of molecular biology

<table>
<thead>
<tr>
<th></th>
<th>Hologic Panther Aptima</th>
<th>BioFire FilmArray RP2.1</th>
<th>Abbott ID NOW</th>
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</thead>
<tbody>
<tr>
<td>Corner Name</td>
<td>COVID-19 Amplified RNA</td>
<td>BioFire Respiratory Panel</td>
<td>COVID-19 Rapid</td>
</tr>
<tr>
<td>Amplification Technology</td>
<td>Transcription-mediated</td>
<td>Multiplexed real-time PCR</td>
<td>Isothermal amplification</td>
</tr>
<tr>
<td>Sensitivity(^1)</td>
<td>600 NDU/mL</td>
<td>6,000 NDU/mL</td>
<td>300,000 NDU/mL</td>
</tr>
<tr>
<td>Turnaround Time, average (95%)(^2)</td>
<td>12.2 h (22.4 h)</td>
<td>2.5 h (4.2 h)</td>
<td>1.4 h (3.2 h)</td>
</tr>
<tr>
<td>Total tests performed(^3)</td>
<td>15,162</td>
<td>14,695</td>
<td>2,463</td>
</tr>
<tr>
<td>Relative Cost to Patient</td>
<td>$</td>
<td>$5555555 $</td>
<td>$</td>
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</table>

\(^1\)Analytical sensitivity determined by FDA; NDU = nucleic acid amplification test detectable units
\(^2\)Turnaround time from receipt for samples received 1/19/21 – 2/22/21
\(^3\)As of 2/22/21

Reporting Ct Values
- Ct is the threshold cycle (the cycle number at which a sample becomes positive)
- Ct is inversely proportional to the target concentration of the sample
  o Higher Ct = lower concentration
- Some studies correlate Ct with disease severity, leading providers request that labs report Ct
- Many challenges in reporting Ct
  o Some assays don’t report Ct (none of ours do)
  o Ct on one assay may not equate to Ct on a different assay
- Multiple assays are in use at many institutions
  o Local studies required to validate Ct cutoffs (different assays, different populations, etc.)
Most commercial assays for SARS-CoV-2 have not been designed to be quantitative
- Ct reflects the concentration of the sample, which is subject to preanalytical issues:
  - Effectiveness of collection
  - Appropriate handling of specimen
  - Uniformity of transport medium volume
- Controls are needed to compensate for these issues for quantitative reporting.
- UMC does not report proxies of SARS-CoV-2 virus concentration
- For assays reporting Ct values, those values should not be used to guide patient management because meaningful correlations among viral assessment parameters have not been established for qualitative SARS-CoV-2 tests. Furthermore, sample, patient, reference material, regulatory, and analytical variables confound efforts to meaningfully correlate Ct values.

**Rapid Antigen Testing**
- Speed, waived status, and relatively low expense are attractive for daily/weekly screening activities (e.g., schools)
- Higher rate of false negatives than nucleic acid methods limits utility in a clinical setting
- Negatives must be correlated to clinical presentation and should be confirmed by nucleic acid testing in symptomatic individuals
- Not currently in use at UMC

**Antibody Testing**
- Useful for identifying previous exposure to SARS-CoV-2
- Not useful or approved for diagnosing infection
- Not useful for evaluating vaccine response
  - Most assays are qualitative
  - Protective antibody concentration has not been established

**Q&A: SARS-CoV-2 Variant Testing**

**What are variants?**
- Viruses mutate constantly; RNA viruses like SARS-CoV-2 mutate faster
  - RNA replication is "error-prone"
- Some mutations hurt the virus' ability to replicate or infect; these mutations are lost due to natural selection
- Some mutations are neutral and may be found sporadically
- Some mutations are beneficial to the virus' ability to spread or cause disease; when these persist or begin to represent a rising proportion of infection, strains with these mutations become known as variants

**Why are variants important?**
- Variants may behave differently than the original virus.
  - More infectious
  - More severe disease
- Variants may not be recognized by antibodies generated to the original virus.
  - Possible reinfection of patients who already had SARS-CoV-2
  - Possible that convalescent plasma treatments will be less effective
  - Possible that vaccines will be less effective
- Variants may not be detected by assays if mutations occur in specific locations recognized by the assay.

**Why do we send for variant testing?**
- Identifying variants through surveillance is an important public health function. Knowing what strains are circulating and in what numbers can help determine whether vaccines are effective against them or whether people who have had SARS-CoV-2 infection previously are susceptible to infection by the variant strains.

**What are the currently known variants?**
- Variants are an ongoing concern. The longer SARS-CoV-2 infections remain widespread, the more likely additional variants will arise.
- As of February 25, there are three major variants of concern. Each has a name based on its genetic relationship to other strains as well as an informal name based on its original geographic association:
  - B.1.1.7 (the "UK" variant)
  - B.1.351 (the "South African" variant)

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**Tecan Tip Alternative Approved**

In response to shortage of Tecan disposable pipette tips for the Panther, Hologic validated Biorear Quaero Filtered Tips as a suitable replacement. The UMC Microbiology Department verified the performance of these tips in early February and will use them to help ensure uninterrupted performance of SARS-CoV-2 testing and other testing performed on the Panther.
- P.1 (the "Brazilian" variant)
- On February 25, media began reporting that a new variant, B.1.526 may be emerging in New York City. It remains to be seen whether it will become a major variant of concern.

**How do we send for variant testing?**
- Providers of patients with appropriate indications can request variant testing.
  - As of February 25, the El Paso Department of Public Health is accepting specimens from patients with suspected reinfections from SARS-CoV-2.
  - On a case-by-case basis, specimens from vaccinated individuals may also be accepted.
- Providers should complete the El Paso DPH Genetic Sequencing Request form and submit it with their patient’s specimen. Only one specimen is required.

**Is it important to know whether an individual patient has a variant?**
- No. Knowing the identity of a patient's strain is not needed to treat patients at this time, and we do not anticipate receiving individual patients' results from the SDHS laboratory.
- Knowing an individual's current strain cannot conclusively prove that the patient was reinfected by a different strain unless the original strain is also known.
- For now, if a patient has a variant, it can be presumed that their original infection was due to the "non-variant" strain.
- As variants enter our region, this presumption becomes invalid.
- Knowing that a vaccinated individual has a variant does not prove that the vaccine did not work against the variant.
- Current vaccines are about 95% effective, which means that they'll stop up to 19 of 20 severe SARS-CoV-2 infections; however, that leaves 1 case that isn't stopped.
- Only by collecting aggregated data from vaccinated individuals can we determine that vaccines do or do not protect against variants.

**What do we know about variants in our region?**
- As of February 18, the SDHS laboratory had not identified any of the current variants of concern from our public health region.
- Across Texas, 60 cases of B.1.1.7 (the "UK" variant) and 1 case of B.1.351 (the "South African" variant) had been identified.

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**III B. Clinical Pathology: Transfusion Medicine/Coagulation**

**Mass Transfusions in the Setting of RBC Antibodies**

**Dr. Jesse Qiao**

**Case presentation:**
- 69 year old female with history of hypertension and hypothyroidism
- Presents with multiple hematemesis episodes
- Hemoglobin was 8.1 g/dL, normal INR, platelets were 87,000 /μL; blood type resulted as O+
- Administered 3 units of emergency release, uncrossmatched O positive RBCs
- Rapid decompensation and hemodynamic instability due to severe ongoing hemorrhage activated the massive hemorrhage protocol

The blood bank began to thaw plasma in anticipation of an emergent need for massive transfusion. During this time, testing revealed a positive antibody screen, demonstrating Anti-C and Anti-E. Therefore, the clinical team waited for antigen-compatible blood rather than administering uncrossmatched O positive blood. Before additional blood products were delivered, the patient was unresponsive and expired.

**Table 1:** Lab values after transfusion of the three O+, uncrossmatched blood:

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>White Blood Count</td>
<td>9.13 x 10³/mm³</td>
</tr>
<tr>
<td>Hemoglobin (no hemolysis)</td>
<td>8.1 g/dL (low)</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>25.2% (low)</td>
</tr>
<tr>
<td>Platelets</td>
<td>81 x 10³/mm³ (low)</td>
</tr>
<tr>
<td>Potassium</td>
<td>4.2 mmol/L</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.6 mg/dL</td>
</tr>
<tr>
<td>Bilirubin total</td>
<td>0.90 mg/dL</td>
</tr>
<tr>
<td>INR</td>
<td>1.4 (high)</td>
</tr>
<tr>
<td>Partial Thromboplastin Time</td>
<td>30.8 seconds</td>
</tr>
</tbody>
</table>
Fibrinogen level  |  118 mg/dL (low)  
| Direct Antiglobulin Test (DAT) | Positive, polyspecific  

Phenotyping showed that two of the three transfused units were positive for the C and E antigens (crossmatch incompatible). While a transfusion reaction workup was not ordered, there was concern that transfusion of the incompatible units may have led to death of the patient.

How are massive transfusions different from routine blood transfusions?
- Heavily regulated: Food and Drug Administration (FDA); College of American Pathologists (CAP); American Association of Blood Banks (AABB).
- Routine, non-emergent circumstances, workups are performed prior to receiving blood products.
- Approximate time for a patient to receive crossmatched compatible blood after ABO/Rh negative screen is 90 minutes.
- O+ RBCs and AB plasma is used prior to uncrossmatched testing in emergent requirements.

Due to blood bank time constraints in preparing products (e.g. fresh frozen plasma), compatibility testing is not usually performed as part of an emergent massive hemorrhage protocol. Blood bank product preparation continues until the clinical team stops the massive hemorrhage protocol.

What should have been done differently in the immediate clinical course of this patient, to better meet transfusion requirements?
- Accept uncrossmatched donor products (O+ RBCs and AB FFP) vs. waiting for C and E antigen negative units from the blood supplier.

How are Anti-C and Anti-E RBC antibodies addressed in the context of mass transfusion?
- About 15-20% of the Caucasian donor population (50-60% in African American) are negative for both the C and E antigens.
- About half of O+ RBC products contain either the C or E antigens (i.e., are incompatible).
- Anti-C and Anti-E (typically acquired by prior transfusion and/or pregnancy) are IgG and compatible.

What additional laboratory workup could include or exclude hemolysis?
In this case, the comprehensive metabolic panel (potassium, bilirubin, and creatinine) was within normal limits. A direct antibody test demonstrated positivity for IgG. A more comprehensive assessment of hemolysis could have been assessed by the following:
- A formal transfusion reaction workup, including a post transfusion type and screen, urine specimen, and return of the units for compatibility testing.
- Lactate dehydrogenase (LDH)
- Haptoglobin
- Serial hemoglobin and hematocrits to monitor

**Should there be concern for a hemolytic transfusion reaction as the cause of death?**
This is not likely because hemolysis was not identified in the post-transfusion H&H sample. While other labs were within normal limits, haptoglobin, LDH, and a post transfusion urine sample were not ordered. This makes it difficult to completely rule-out hemolysis.

Because the Anti-C and Anti-E RBC antibodies are IgG, they do not cause intravascular hemolysis that is usually caused by IgM antibodies (mostly ABO) that can lead to devastating clinical consequences and metabolic derangements. Because the patient decompensated during a few hours, extravascular hemolysis due to Anti-C and Anti-E would be too soon for significant symptoms to develop.

It is important to remember that a positive DAT alone does not equate to hemolysis. It only means that the patient has bound antibodies to red blood cells. With the presence of Anti-C, Anti-E, and a positive DAT, if there is no clinical or laboratory evidence of hemolysis after several days, then the scenario would be best classified as a delayed serologic (rather than hemolytic) transfusion reaction.

**References**
Jesse Qiao, M.D.; Sectional Director, Blood Bank and Transfusion Services at University Medical Center El Paso Laboratory Medical Director, the Hospitals of Providence at Transmountain jesse.qiao@ttuhsc.edu

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**III B. Clinical Pathology: Test ordering and Interpretation**

**When is a cholesterol test better than a $5,000 send-out?**
Dr. Jude Abadie

When I was stationed Walter Reed Army Medical Center several years ago as medical director of clinical chemistry, I opened my email to see “Long QT Test” as the Subject-Line in a string of emails. Here is an abbreviated transcript summarizing the e-mail progression.

**Cardiologist #1:** Dear lab, I’m the doctor for a 22-YO Army Soldier whose ranger school admission electrocardiogram (ECG, routine screening component for this school) showed a long QT with no obvious reason or family history.
- The Army will deny the ranger school admission packet if his ECG abnormality is caused by a cardiac channelopathy.
- Therefore, I'm requesting approval for genetic testing to identify a mutated gene responsible for a cardiomyopathy and ion channel arrhythmogenic disease known as familial long-QT syndrome (LQTS).
- On this e-mail, I’m including the cardiologist who ordered this same assay for another patient last year. Please approve this test for my patient.

**Cardiologist #2** (Cardiologist who ordered this test last year): Yes. The test result was critical in deciding cardiac defibrillator implantation.
- While we have tested only that 1 patient for LQTS genes, the assay is probably underutilized due to lack of availability.
- I am including other cardiologists on this e-mail to solicit thoughts related to the utility of this test.

**Cardiologist #3:** This test would likely be ordered 5 times a year by our group, but I suspect pediatric cardiologists would order it even more (10 to 15 per year).
- Dear pediatric colleagues cc’d here: “How many familial LQTS tests would you order per year?”

E-mails #4 and #5 concurred with the preceding cardiologists’ remarks and attached an article reviewing LQTS genotype influences on medical outcomes as well as an article reviewing genetic testing for channelopathies. A final e-mail (from cardiologist #6) summarized the cardiologists’ decision for increased utility of this test.

When summing the proposed testing usage, the cardiologists suggested that this $5,000 send-out test would be ordered about 20 times per year, requiring an additional $100,000 contract. Interestingly, throughout the entire history at the hospital, the LQTS test had been ordered only once.

The cardiologists obviously view the LQTS genotype assay as an important test to improve patient care. Perhaps they believe this sophisticated test will be a powerful diagnostic tool, making the hospital more prestigious and improving its status as a center of excellence.
After all, the assay results proved to be lifesaving in the hands of cardiologist #2 during the previous year. After reading those e-mails, how does a laboratory professional proceed to address this request?

The requesting providers saw the LQTS molecular assay as a valuable tool for patient care. How does a laboratory address this request?

- Literature review suggested that LQT genetic analysis contributed to confusion about realistic expectations for testing applicability of cardiomyopathies and ion channel diseases.
- One publication sent by the cardiologists discussed difficult roles of genetic analysis in the management of ion channel diseases and cardiomyopathies.

Table 1 lists clinical questions to answer before considering approval for expensive molecular testing.

With respect to the LQTS test and this case, the 2 questions appearing most relevant are related to outcome effects on medical management and subsequent family member follow-up testing, especially if the primary patient result is positive.

A truism for new drugs: After a new drug is released to market, its side effects will increase over time.
- My mother’s thyroid medication literature warned about stomach discomfort.
- She claimed additional side-effects not listed (headache, breast pain, fatigue, and anxiety).

- She implicated the thyroid pills for these “ailments” and was wondering if it could cause bluish tint to hair color as her mother had when she was on the same medication.
- At that time, perhaps a simple cholesterol test would have been the best test to order to address concerns.
- A normal result, because of the implications of a normal cholesterol screen, could likely decrease anxiety as well as other perceived side effects.

A truism for new lab tests: After a new assay is released to market, its specificity will decrease and its use will increase over time. These 2 variables are closely linked. Anxious patients can convince themselves and their physicians that they have some disease process that can be detected via a lab test.

Figure 1 shows that prevalence is highly dependent upon an assay’s predictive positive value (PPV). For example, with a constant sensitivity of 95% and a low pretest probability (PTP), there is very little diagnostic value added, despite an increase in specificity from 75% to 95%. Perhaps random or obscure assay ordering is the worst service a patient can receive when a disease PTP is low, irrespective of assay performance. In such cases, a cholesterol test may better benefit the patient by better predicting risk for a more likely disease state.

- When prevalence/PTP is low, false-positive screening tests can be dangerous.
- Harm can be caused by worry, unnecessary diagnostic procedures, and treatment.
- Few evidence-based recommendations exist for ordering even the most common laboratory test in asymptomatic adults with no family history. For example, no evidence exists for ordering a chemistry panel, a CBC, TSH, CA-125, or a urinalysis in a “normal” population.
- Glucose ordering is debatable and limited to some pregnant women and individuals older than 45 years of age.¹
- Routine prostate specific antigen (PSA) as a screen has been controversial.

Perhaps differences in opinions for PSA screening are related to reports of very low death rate (0.2%) from prostate cancer versus reports suggesting that prostate cancer eventually becomes ubiquitous in all men. With enough needle biopsies, a study on postmortem samples in trauma deaths states that prostate cancer is often found in otherwise healthy men in their 20s.² This can lead to testing confusion in cases where there is little evidence suggesting that intervention improves outcome.³

Perhaps a gold standard screening test, as some may consider a cholesterol test, would not only be less expensive but also a better predictor of long-term risk for preventable cardiovascular disease.

While guidelines serve important roles for ordering laboratory tests, there is no substitute for logical, individual case assessment. Here are 5 practical tips (also summarized in Table 1) to keep in mind when considering a test order or seeking pathology approval for a potentially obscure test:

1. Before ordering a test, ask how the treatment outcome will differ if the test result is positive or negative. If answers are the same, order a cholesterol test. A cholesterol test may be more likely to generate a better treatment decision.

2. Do not order tests without a diagnostic history or investigation plan. Such testing is referred to as “fishing expeditions.” In lieu of such expeditions, a cholesterol test is less likely to generate confusion.

3. If a test requires pathologist approval, there is about a 30-40% chance it is not needed (personal observations). A cholesterol test might be a better choice and generate less worry.

4. Beware of using a third party to order tests. “I told the medical assistant to order a free T4, but the laboratory performed a free testosterone.” In this case, a testosterone result may generate unnecessary concern and be less useful than if the communication error had instead generated the order for a cholesterol test.

5. Sometimes, ordering the same test again will solve the problem, especially when considering analytical and inter-individual variations.

- Several years ago, my father’s cholesterol was 198 mg/dL; he was quite happy with this result because anything < 200 mg/dL was “normal.”
- A few years later, his cholesterol was 203 mg/dL, and he was horrified with that result. The day after learning this value, he had chest pain, stomach cramps, and some dizziness.
- Perhaps the best medical service my father could have received to “cure” his chest pain would have been for his clinician to order another cholesterol test.
- In such instances, a repeat test has a high probability of being “normal.”

What does it mean when the PTP is high and a laboratory test result is out of the reference range? Remember, there are only 3 causes for an abnormal result.

1. Some healthy people have abnormal results. Based on the normal distribution with a 95% confidence interval, there is a 30% chance of having 1 abnormal result on a Chem-7 from a “normal” healthy individual (1 – [0.95]² = 0.30).

2. Abnormal results are sometimes erroneous. While the laboratory may sometimes like to dismiss this cause, preanalytic, analytic, and postanalytic errors account for a well-recognized proportion of abnormal results.

3. The disease in question can cause an abnormal result and is attributable, especially when PTP is highest.

While some salient characteristics presented here may seem obvious, they can be lost somewhere among the lab, residents, and attending clinicians. While it is the clinicians’ responsibility to ensure that the highest PTP supports the test orders, the lab is responsible for providing appropriate guidance for testing services.

So, what happened with the 22-year old Army Soldier and his application to ranger school?

- When considering future medical insurance implications that could precipitate from disclosing a positive LQTS test, the soldier decided it...
would be best to forgo ranger school and genetic testing, and not know his channelopathy status, thus keeping the result out of his medical record.

- The cardiologists also realized that the novel and valuable familial LQTS test should be reserved for those rare cases where results would have an effect on treatment decisions in patients with a high PTP.
- By making the decision to forgo the $5,000 send-out LQTS test, the soldier essentially opted to let a more natural course of events transpire, such that when the time comes for purchasing an insurance policy, an insurance company would base coverage decisions on a different, less sophisticated or pretentious test. Yes, this will be a cholesterol test!

Laboratory-related patient care will continue to become more efficient when considering these test ordering philosophies.

Perhaps one day each clinician will have a story to tell where a better patient outcome resulted from ordering a cholesterol test.

References:
4. Abadie, JM. Laboratory perspectives on test ordering and interpretation: or when is a cholesterol test better than a $5,400 send-out? LABMEDICINE, 38:7, Jul 2007.

IV. The Laboratory Use Committee (LUC). . . A new initiative

Dr. Jude Abadie

The pathology department has established the Laboratory Use Committee (LUC). The LUC considers all requests for new testing implementation and actionable items related to approvals for send-out tests.

Purpose: Improve our ability to provide the most valuable clinical testing services in efforts:

- To maximize safe, expert patient care through identification, implementation, execution, and interpretation of the most appropriate testing in support of provider services for the right patients at the right time.

Committee members include the committee chair who is the Director of CP, Director of Microbiology, four pathologists, as well as UMC and TTUSHC senior lab managers.

Action items are processed as follows:
- Requests should come from providers with rank of Assistant Professor, Associate Professor, or Professor.
- The LUC Chair will document the written request and communicate the review process to the requesting department.
- A date will be set when the request will be reviewed and decided upon by the LUC. The requesting department will present their formal request during this meeting.
- A completed justification packet will be distributed to our LUC group two weeks prior to the meeting.
- Decisions and follow-through will occur one week after each LUC meeting, when written notice is provided to the requesting department.
- Secondary LUC functions include reviews of in-house testing operations and logistics for clinical and managerial based on needs/requirements identified within our pathology department.
- Action items for implementation will be coordinated with UMC and TTUHSC management.

Change to be implemented on 12 April 2021

During our first LUC meeting in February 2021, we reviewed the process for pathology approvals of send-out tests. Send-out tests that cost more than $750 require pathology approval. To help pathology with this process, a form with the salient information must be completed as described below:

- General information that includes the test name and requesting providers information
- The clinical indication why the test is required
- Explanation of how results of the test will change clinical management of the patient
- List of other tests that have been ordered or considered to address the clinical presentation and why those are insufficient.

The form can be completed by any provider but must be signed by the attending provider when the request comes from a resident.
Goals of this process include helping to guide more expensive test requests in the context of:
- Pretest probability
- Being stewards of funds
- Supporting providers to provide optimal care for their patients

When reviewing send-out requests, pathology will consult with the specialists in our department to support the guidance and intentions stated above.

The next iteration of this Path-O-Gram will detail the process for reviewing and investigating send-out requests for some molecular testing. Additionally, it will present specific examples for the utility of genetic testing for both tumor/cancer as well as constitutional analysis.

As this processes is implemented by pathology, we look forward to working with providers to discuss any aspects of requests so that the best decisions can be made for our organization and for our patients.

Feel free to direct related questions to Dr. Jude Abadie at jude.abadie@ttuhsc.edu and/or at 915-215-4956.

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**Announcements: Test discontinuation**

**Dr. Jude Abadie**

**Effective April 5, 2021**, the core laboratory will no longer offer bleeding time testing.
- The bleeding time test (BTT) is an antiquated assay whose assessment is better evaluated by coagulation tests.
- The relationship between the BTT and the risk of a patient’s actually bleeding has not been established.
- This position is supported by the American Society for Clinical Pathology in a statement they initially released in 2013. The BBT is an outdated assessment used to evaluate platelet function and vascular integrity.
- BTT is highly operator-dependent, lacks reproducibility, and is confounded by technical factors such as incision location, pressure applied, and patient factors (age, gender, diet, hematocrit, skin laxity, and medications).

A careful clinical history (family, dental, obstetric, surgical, traumatic injury, transfusion, and drug history) is recommended for initial screening.
- Positive clinical history should be followed with screening tests of coagulation (PT and APTT), a platelet count, and ruling out von Willebrand’s disease (Factor VIII, von Willebrand Factor Antigen, Ristocetin Cofactor). If these tests are negative, a platelet function disorder can be investigated with platelet aggregation testing.

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**Effective January 11, 2021**, the microbiology section at UMC discontinued testing for respiratory viruses by direct fluorescent antibody (DFA).
- After the introduction of the BioFire FilmArray Respiratory Panel 2.1, orders for DFA testing decreased to almost nil.
- This reduction made it impractical to maintain the test.
- The BioFire panel identifies all DFA targets as well as additional targets not previously tested at UMC.

Direct questions to Dr. Aaron Geno at 915-215-4956 or k.aaron.geno@ttuhsc.edu

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Thank you for taking the time to review our Path-O-Gram!