

## Pathology & Laboratory Medicine

# Communiqué

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### TEST CATALOG

To view a complete listing of available Tests, please visit

**[UVMLabs.TestCatalog.org/](http://UVMLabs.TestCatalog.org/)**

Browse by Name Search

A B C D E F  
 G H I J K L



### LAB OPERATIONS



## Zika Virus: How to order Testing

Ordering providers must call the Vermont Department of Health (VDH) Infectious Disease Epidemiology at 802-863-7240. VDH is filtering patients to determine risk level and if testing is appropriate.

In addition to patient demographic information, doctors must provide:

1. Travel History
2. Exposure history
3. Symptom history and date of onset (if applicable)
4. Pregnancy status (if applicable)

### Fill out the VDH Clinical Test Request Form

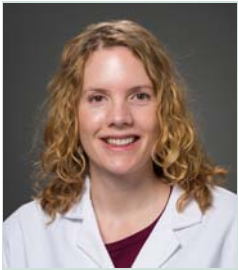
The patient must have an order for the Zika Testing (PRISM, Laboratory Order Form, Atlas, etc.) and the completed VDH form. Phlebotomy will **not** collect without the VDH form,.

### CRITERIA FOR ZIKA TESTING

- Any symptomatic\* person with travel to an area with active Zika transmission within previous 2 weeks of symptom onset, **OR**
- Any symptomatic\* person who had unprotected sexual exposure to semen of a man\*\* who had previously traveled to an area with active Zika transmission, **OR**

*\*Symptoms consistent with Zika virus include acute febrile illness, rash, arthralgia, conjunctivitis, myalgia or headache*

(Continued on page 15)



Suzanne Tucker, MD  
 Medical Director  
 Autopsy Service  
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## New Medical Director of Autopsy Service

Dear colleagues,

This is a belated announcement that Dr. Suzanne Tucker is our new Director of the Autopsy Service beginning on July 1<sup>st</sup> following the retirement of Dr. Brenda Waters. Dr. Tucker joined our department as an Assistant Professor of Pathology specializing in Pediatric Pathology and Autopsy Pathology as well as Neuropathology and Bone and Soft Tissue Pathology in September of 2013. She completed her medical education at the University of Nebraska Medical Center followed by her AP/CP residency in Pathology here at the University of Vermont Medical Center. She subsequently trained as a fellow at Boston Children's Hospital in Pediatric Pathology. Dr. Tucker has board certification in Anatomic Pathology, Clinical Pathology and Pediatric Pathology. She has shown great dedication and interest in Autopsy Pathology and has already shown to be an excellent teacher in this arena. We are very lucky to have Suzanne as the new leader in Autopsy Pathology and thank her for her energy and leadership in this important subdivision of our department!

Warm regards,

Mark Fung

Mark K Fung, MD PhD FCAP  
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 and Medical Laboratory and Radiation Sciences  
 Univ of Vermont Colleges of Medicine, Nursing and Health Sciences  
 Director of Clinical Laboratories  
 Director of Transfusion Medicine Services (Blood Bank, Stem Cell, HLA)

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## HLA Disease-Related Testing Update

Due to unforeseen circumstances, effective Monday, October 3 2016, the following disease-related HLA tests will temporarily be performed at Mayo Medical Laboratories, Rochester, MN, instead of at UVM-MC.

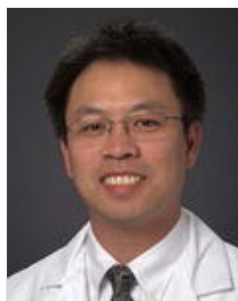
- HLA B27 screen (MB27) – will be sent to Mayo for analysis (Mayo Test ID LY27B – UVMHC order code B271)
- Celiac HLA DQ A,B (CELIDQ) – will be sent to Mayo for analysis (Mayo Test ID CELI – UVMMV order code CELIDQ1)
- HLA B type (MHLAB) – will be sent to Mayo for analysis of either HLA B 5701 Genotype, Abacavir Hypersensitivity (Mayo Test ID HLA57 – UVMHC order code B5701G) or HLA B High Resolution (Mayo Test ID FHLAB – to be ordered as a miscellaneous test)

Result turn-around time will not be affected by this change.

All other HLA tests offered through our laboratory are unaffected by this change.

We apologize for any inconvenience this change may cause, and anticipate being able to offer these assays again in the near future.

If you have questions, please contact Dr. Mark Fung ([mark.fung@uvmhealth.org](mailto:mark.fung@uvmhealth.org)) in the Laboratory.



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## APT Test Inactivation

Due to decreased test volume the APT test will be inactivated on October 24, 2016. Should this test be required, we can send the testing to Mayo Medical Laboratories.

Please direct any questions to John Lunde, MD (John.Lunde@UVMHealth.org) in the Hematology Laboratory.

## Extended Platelet Expiration Date From 5 to 7 Days

The AABB Blood Bank & Transfusion Services Standards (30th Ed. 2016) revised by Association Bulletin #16-05 and the FDA Draft Guidance for Industry 2016 – Bacterial Detection Testing by Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion, allow an extended expiration date (from a Day 5 expiration to Day 6 and Day 7 expiration) for leukocyte reduced apheresis platelets when they are appropriately labeled as bacterial screen test negative using a bacterial detection device cleared by the FDA as a “safety measure.”

The Pan Genera Detection (PGD) test from Verax Biomedical is the only bacterial detection device cleared by the FDA as a “safety measure” at this time. The University of Vermont Medical Center Blood Bank will use the PGD test to extend the expiration date of platelets up to 7 days. The use of Day 6 and Day 7 platelets was approved by the Transfusion Committee in April 2016. Labeling of Day 6 and Day 7 platelets will be performed in the Blood Bank and will not affect the processes of ordering, issuing or transfusing blood products.

Please direct additional questions to Sarah Harm, MD, Medical Director of Blood Bank, sarah.harm@uvmhealth.org or 802-847-2384.

## Thrombosis Panels (TP and TP1C) Change

Please note the Thrombosis and Hemostasis Laboratory no longer offers the Factor V Leiden molecular-based assay (FACT5L) as part of any thrombosis panel. To screen patients for a Factor V Leiden mutation, the Activated Protein C Resistance assay (APCR) has been added to the thrombosis panels (TP1 and TP1C). The APCR assay is a clot-based test which is sent Mayo Medical Laboratories for testing.

As of 9/12/2016 the Prothrombin Gene 2010A Mutation assay (PROGMU) was also removed from the thrombosis panels (TP1, TP1C and NONPRG ). There is no alternate clot-based assay available.

Both the Factor V Leiden and Prothrombin 2010A Gene Mutation molecular-based assays remain available for ordering as separate tests.

**The Factor V Leiden and the Prothrombin 2010A Gene Mutation molecular-based assays now requires pre-authorization from non-Medicare insurers.** If prior authorization is denied, a Notice of Patient Potential Financial Responsibility form will be required. The Advance Notice of Potential Non-coverage by a commercial payor form is available on our website.

Medicare will not cover this testing. The UVMHC Laboratory will require a signed Advanced Beneficiary Notification (ABN) form for all Medicare patients for this testing. This ABN informs the patient that they are financially responsible for the cost of the testing if their medical insurance denies payment. [The ABN is also available on our website.](#)



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## New Test for Indeterminate Thyroid Nodules Afirma Gene Expression Classifier (GEC)

The Cytopathology Department began offering the Afirma Gene Expression Classifier (GEC) Test starting on August 1, 2016. This test is utilized in the management of patients with indeterminate thyroid nodules.

### CLINICAL APPLICATION:

Approximately 525,000 thyroid nodule Fine Needle Aspirations (FNA) were performed in the United States in 2011.<sup>1</sup> Cytopathology FNA samples can be challenging to interpret. Indeterminate results are generated in 15-30% of the cases.<sup>2</sup> Prior to Afirma testing, guidelines recommended that most of these patients undergo surgery to assess whether the nodules were benign or malignant.<sup>3</sup> In approximately 70-80% of the cases the nodules were determined to be benign by surgical pathology.<sup>4</sup> The Afirma GEC reduces the number of surgeries by identifying indeterminate Cytopathology Thyroid FNAs which are low risk for cancer.

### AFIRMA GENE EXPRESSION CLASSIFIER:

The Afirma GEC measures the expression of 142 genes to determine if the thyroid nodule FNA sample is benign or suspicious for cancer. Patients with benign Afirma results can potentially avoid unnecessary surgery. Results will be available in PRISM. Clinical usage of the GEC is supported by clinical practice guidelines such as the American Thyroid Association.<sup>5</sup>

Afirma Gene Expression Classifier	
Division	Cytopathology
Specimen Information	Collect two Thyroid FNA passes in one FNAprotect vial. Appropriate only for indeterminate nodules on rapid evaluation.
Test Priority/Analytical Time/Test Priority	Monday-Friday / 7-10 days / Not available STAT
Method	Gene Expression
NYS Certified	Yes
Effective Date	August 1, 2016

### REFERENCES FOR AFIRMA GENE EXPRESSION:

1. Sosa JA, Hanna J, Lanman RB, Robinson KA, Ladenson PW. Increases in thyroid nodule fine needle aspirations, surgeries and diagnosis of thyroid cancer in the United States, American Association of Endocrine Surgeons 34<sup>th</sup> Annual Meeting, Apr 14-16, 2013, Chicago, IL. (oral abstract).
2. Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. *Thyroid* 2009;19:1167-1214.
3. Gharib H, Papini E, Paschke R, Duick DS, Valcavi R, Hegedus L. et al. American Association of Clinical Endocrinologists, Associazione Medicie Endocrinologi, and European Thyroid Association medical guidelines for clinical practice for the diagnosis and management of thyroid nodules: executive summary of recommendations. *Endocr Pract.* 2010;16(S1): 1-43.
4. Wang CC, Friedman L, Kennedy GC, Wang H, Kebebew E, Steward DL, et al. A large multicenter correlation study of thyroid nodules; cytopathology and histopathology. *Thyroid.* 2011;21:249-251.
5. Haugen BR, Alexander EK, Bible KC, et al. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. *Thyroid.* 2016;26:1-133.

## Spotlight on the Lab: Pathology Residency Training

The Pathology Residency Training program at the University of Vermont Medical Center is composed of a combined Anatomic and Clinical (AP/CP) Pathology program. Some institutions provide training in Clinical Pathology or in Anatomic Pathology alone, but we currently offer only a combined training program. The length and components of the resident's experience is driven by the criteria needed to sit for the certification examination given by the American Board of Pathology - ABP ([www.abpath.org](http://www.abpath.org)). In addition to the experiences required, the ABP also requires all qualifying residency programs to be accredited by the Accreditation Council for Graduate Medical Education - ACGME ([www.acgme.org](http://www.acgme.org)).



Alison Krywaczyk, MD fourth year  
Pathology Resident in the grossing lab

The ABP requires the following training requirements in order to be eligible for the examination:

1. The applicant must have 48 months of full-time training in an accredited AP/CP program
  - a. At least 18 months each of structured AP and CP training
  - b. The remaining 12 months are flexible and may include AP and/or CP rotations
2. The applicant must have completed at least 50 autopsies

Based on the requirements above, you can see that there is a fair amount of flexibility in the way residents are trained. The ABP lets programs design the curriculum and train the resident in a way that best fits the institution where the program is located. In order to insure the quality of the program, the ABP requires that the program be accredited by the ACGME. The ACGME has a set of "Common Program Requirements" that all programs in every specialty must meet. In addition, there are specialty specific requirements that must be met (for example AP/CP Pathology, Cytopathology, Hematopathology, and Dermatopathology). And, as if that is not enough, there are also Institutional Requirements that UVMCC must meet in order to have any residency training programs. At the institutional level, the Pathology residency program is overseen by the Office of Graduate Medical Education, supervised by the Designated Institutional Officer (DIO), currently Mark Levine, MD.

The Pathology residency program at the University of Vermont Medical Center is accredited by the ACGME for 16 residents. Ideally, this would be four residents in each of the four years of residency. All residents have an MD, DO, or equivalent degree, obtained following undergraduate education and medical education. Nearly all residents graduating this program go onto fellowship training, which is typically one year in length. We have four fellowships here at UVMCC, Cytopathology, Dermatopathology, Hematopathology, and Surgical Pathology.

Training future pathologists is a complicated and highly regulated endeavor. One might even say "It takes a village!" Along with attending physicians, the laboratory staff plays an enormous role in training of the residents and their commitment and dedication to this teaching is very much appreciated.

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*"My favorite aspect of working in this department is the collegial atmosphere and the incredible support from attending faculty and staff. This support has enabled me to reach my career goals and make critical professional connections."*

Lauren Pearson, MD – Pathology Chief Resident,  
University of Vermont Medical Center

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## Anti Nuclear Antibody: New Test Codes

The Antinuclear Antibody order code: ANA will be replaced with a new order code: ANAIFA. The new test code, which consists of a battery of tests, will result in a change in how results are reported.

Currently a positive ANA will reflex an ANA Titer (ANAT). The new battery consists of four tests: the ANAIF, which is the overall ANA interpretation and three separate tests available for up to three patterns reported at different titers, if needed. Currently ANA titers are reported as dils which will now be reported as titer. Negative ANA's are currently reported as "<40 dils", but with the new test code will be reported as "Negative. No titer performed, ANA screen is negative."

This change will take effect on Friday 11/04/2016. There is no change in methodology, sample requirements, or sample stability and this is only a change in reporting (Refer to the Laboratory Test Catalog for current information). Positive ANAIFA will still result in a reflex titer being performed at an additional charge. See a sample of current and new sample reports below.

Current Reporting		New Reporting	
Test Code: ANA	PRISM Code: LAB148	Test Code: ANCAIF	PRISM Code: LAB
<b>Negative</b>			
Anti Nuclear Ab <40	[0-40] Dils	Anti Nuclear Ab, IFA ANA Interpretation Negative [NEGAT] No Titer performed, ANA screen is negative.	
<b>Positive (Simple Scenario)</b>			
Anti Nuclear Ab	Positive at 40 dils, titer to follow. [0-40] Dils	Anti Nuclear Ab, IFA ANA Interpretation	<b>A Positive [NEGAT]</b>
ANA Titer	<b>H 80</b> [0-40] Dils Speckled pattern	ANA Titer Pattern	1:80 Speckled
<b>Positive (Complex Scenario)</b>			
Anti Nuclear Ab	Positive at 40 Dils, titer to follow. [0-40] Dils	Anti Nuclear Ab, IFA ANA Interpretation <b>A Positive [NEGAT]</b> For titers greater than or equal to 1:160 (except the centromere and nucleolar patterns) it is recommended that specific, follow-up autoantibody testing (such as for dsDNA and Extractable Nuclear Antigens) be performed on all diffuse and/or speckled patterns.	
ANA Titer	<b>H 640</b> [0-40] Dils Nucleolar pattern Diffuse pattern seen at 320 Dils Speckled pattern seen at 80 Dils	ANA Titer Pattern 1:80 Diffuse, Speckled and Nucleolar ANA Titer Pattern 2 1:320 Diffuse and Nucleolar ANA Titer Pattern 3 1:640 Nucleolar	

### ANCAIF REPLACES ANCA TEST CODE

The Anti-Neutrophil Cytoplasmic Antibody order code: ANCA will be replaced with a new code: ANCAIF. This change was necessitated by the implementation of a new interface that will streamline how this test is resulted in the laboratory and eliminate the inherent error in manual entry. The new test code which consists of a battery of tests will result in a change in how results are reported.

Currently a positive ANCA will reflex an ANCA Titer (ANCAT). The new battery consist of three tests: the ANCAI, which is the overall ANCA interpretation and two separate tests available for up to two patterns reported at different titers if needed. Currently ANCA titers are reported as dils which will now be reported as titer. Negative ANCA's are currently reported as "<20 dils", but with the new test code will be reported as "Negative. No titer performed, ANCA screen is negative".

(Continued on page 7)

This change will take effect on Friday, 11/04/2016. There is no change in methodology, sample requirements, or sample stability and this is only a change in reporting (Refer to the Laboratory Services Directory for current information). Positive ANCAIF will still result in a reflex titer being performed at an additional charge. In addition, all Perinuclear Patterns (P-ANCA) and Cytoplasmic Patterns (C-ANCA) will reflex both a Myeloperoxidase Antibody test (Order code: MYL) and a Proteinase 3 Antibody test (Order code: PR3AB) sent to Mayo Medical Laboratories. See a sample of current and new sample reports below.

Current Reporting	New Reporting
<p><b>ANCA</b> &lt;20 [<math>&lt;20</math>] Dils ANA Positive. Suggest follow-up ANA testing if clinically indicated. Cannot rule out Atypical ANCA (A-ANCA).</p>	<p><b>ANCA, IFA</b> ANCA Interpretation Negative [NEGAT] (404) ANA Positive, suggest follow-up ANA testing if clinically indicated. Cannot rule out Atypical ANCA (A-ANCA). No titer performed, ANCA screen is negative.</p>
<p><b>ANCA</b> Positive at 20 Dils, titer to follow [<math>&lt;20</math>] Dils</p>	<p><b>ANCA, IFA</b> ANCA Interpretation <b>A Positive</b> [NEGAT] ANCA Titer Pattern 1:640 Perinuclear Pattern</p>

## Calcium and Albumin Calibration Result Bias

A number of clinicians have noted an apparent increase in the number of patients they see with elevated calcium values. This has been particularly striking when the “calculated” calcium is considered. This is due to two effects, both as a result of a regular recalibrations due to a change in reagent lots on the biochemistry analyzers used in the Chemistry Laboratory. These changes took place at the end of May.

The first change is an increase in the calcium calibration which the manufacturer indicated was to correct a lower calibration that had been seen in the previous lot of reagents. Thus, the change in reagent lots resulted in a larger change in calcium than would normally be noted.

The second change is an apparent decrease in the calibration for albumin with a change in reagent lots that occurred at about the same time. Given the formula for “calculated” calcium, this would cause an additional increase in the reported calculated calcium values.

For most patients these changes should not have a clinically significant effect. However, for patients who are close to the high end of the reference range, these changes could result in the determination of a calcium level outside the reference range, particularly when considering the “calculated” calcium.

In the short term we have no way to change these calibrations in a significant fashion. We are considering the possibility of a change in the reported reference range: however, this could be an issue with another change in reagent lots. In the short term, therefore, we would request that caution be exercised in considering a patient to have hypercalcemia, especially when considering the “calculated” calcium. If you have questions concerning this issue please contact Dr. Greg Sharp ([gregory.sharp@uvmhealth.org](mailto:gregory.sharp@uvmhealth.org)) in the Chemistry Laboratory.

### PATIENT INSTRUCTION BROCHURES

We have several brochures for patients that need to collect samples at home. To view the brochures use the links below or online by visiting <http://uvmlabs.testcatalog.org/> or you can contact Lab Customer Service to receive some via mail.

- [Feces Sample Collection](#)
- [Fecal Occult Blood Collection](#)
- [Sputum Sample Collection](#)
- [Urine Sample Collection](#)

## Calculated Calcium Formula Change

Calcium can bind to serum proteins but it is the unbound calcium that is thought to be physiologically active. Various formulas have been used to attempt to account for the measured total calcium and the amount of protein, predominantly albumin, present in the blood. The formula that has been used at UVMHC for many years has been:

$$\text{calculated calcium} = \text{measured total calcium} + (4.4 - \text{albumin})$$

Given that the average albumin measured in UVMHC is closer to 4.0 than 4.4 this formula tends to show an increase in calculated calcium for most patients that may not necessarily reflect their physiological calcium status. Recently, when a change in lot number for albumin and calcium reagents tended to decrease the albumin and increase the measured total calcium it became apparent that this formula resulted in a significant increase in patients having calculated calcium levels outside of the normal range that did not have hypercalcemia.

Therefore, in order to better reflect the average albumin and somewhat buffer the effect of this correction, a **new formula**, will be used:

$$\text{Calculated calcium} = \text{measured total calcium} + (4.0 - \text{albumin}) * 0.8$$

As can be seen, this will result in a significant change in calculated calcium levels, but is a better “correction” than the previous formula. This change took place on October 5, 2016. A comment: “change in formula for calculated calcium on October 5” will be added to each result for 6 months. Ordering and resulting codes will not be changed.

If you have any questions concerning this change please contact Dr. Greg Sharp ([gregory.sharp@uvmhealth.org](mailto:gregory.sharp@uvmhealth.org)) in the Chemistry Laboratory.

## Endomysial Antibody NOT Recommended

While a number of tests are available to aid in the diagnosis of celiac disease (CD), it is often difficult to know when these tests are appropriate and if they add additional information concerning the patient’s disease state or would change treatment or disease management.

A review of current published literature suggests that IgA anti-endomysial antibody testing (EMA), an Immunofluorescent assay, has limited clinical utility. Although EMA has a specificity and sensitivity of >95%, it has been suggested that EMA is less sensitive, especially among celiac children under two years of age, as well as in the elderly population. In addition, it has been reported that false negative EMA results may be associated with milder small-bowel mucosal lesions. Despite the high accuracy of EMA, it has the distinct disadvantages compared to other serologic tests in that it is expensive, subjective, and labor-intensive, requiring experienced personnel to perform. The technical disadvantages of the EMA resulting in significant inter-observer and inter-site variability have led to the EMA being largely replaced by newer enzyme-linked immunosorbent assays (ELISA), such as the anti-tissue transglutaminase (tTG) and/or anti-deamidated gliadin peptide (DGP).<sup>3</sup>

In 1997, research studies identified the ubiquitous enzyme tTG as the auto antigen, which reacts with EMA, leading to the development of ELISAs that detect antibodies against tTG. tTG assays demonstrated high sensitivity (>95%) and high specificity (>95%) with lower cost and greater reproducibility, due to the advent of automation, than immunofluorescent assays and for these reasons, has become the most common and preferred screening test for celiac disease diagnosis and monitoring.<sup>3</sup>

To confirm these findings our Immunology Laboratory at UVM Medical Center examined the results of patients for whom both IgA anti-tissue transglutaminase (IgA tTG) (SQ Test Code: TTAB) testing and IgA anti-endomysial antibody (SQ Test Code: END) testing were performed.

From January 1, 2015 to June 30, 2016, 369 TTAB and END were both performed on a total of 337 patients. Of these 337 patients, 330 were negative for both TTAB and END, 4 were positive for both TTAB and END, 3 were positive for TTAB and not END, and 0 were negative for TTAB and positive for END as illustrated in the table on page 9.



		IgA Anti-Tissue Transglutaminase Antibody	
Anti-Endomysial Antibody		Neg	Pos
	Neg	330	3
	Pos	0	4

These results clearly indicate that there is little added value of the EMA test in addition to, or as a substitution for IgA tTG testing. Further, since the EMA is considered unreliable in monitoring response to treatment<sup>1</sup>, there may be little indication for repeat testing in this scenario.

With the above data confirming published studies that EMA testing has little diagnostic value and with the consideration that EMA testing is not included in the algorithm for celiac disease (CD) suggested by the American College of Gastroenterology (ACG)<sup>2</sup>, **EMA testing will no longer be orderable as a stand-alone test beginning 10/10/2016.** The test will still be available, as a reflex test only, as part of the Celiac Disease Comprehensive Cascade (Test Code: CDCC) and the Celiac Disease Serology Cascade (Test Code: CDSC) sent to Mayo Medical Labs (MML). However, it is reflexed only when the IgA tTG is weak positive. NOTE: Please refer to the UVMC Laboratory Test Catalog for specific test information including sample requirements, cascade test components, and criteria for cascade reflex testing (<http://uvmlabs.testcatalog.org/>). In keeping with the algorithm used by MML, all weak positive TTAB will include a comment that suggests follow-up testing for anti-endomysial antibodies and/or anti-deamidated gliadin peptide antibodies if clinically indicated. A serum sample will be available for at least seven days for add-on testing if needed. From September 1, 2015 to August 31, 2016, we reported 39 weak positive TTAB results out of 2,337 total TTABs ordered which is a weak positive rate of only 1.7%.

Test Name	Primary Code	SQ Code	PRISM Code
<a href="#">Gliadin Antibody Panel</a>	DGP	DGP	LAB821
<a href="#">Tissue Transglutaminase AB IgA</a>	TTAB	TTAB	LAB723

## REFERENCES

1. James, MW, Scott, BB. Endomysial Antibody in the diagnosis and management of coeliac disease. *Postgrad Med J* 2000; 76: 466-468.
2. Rubio-Tapia A, Hill ID, Kelly CP, Calderwood AH, Murray JA, American College of Gastroenterology. ACG clinical guidelines: diagnosis and management of Celiac disease. *Am J Gastroenterol.* 2013; 108:656-676.
3. Kaswala, DH, Veeraraghavan, G, Kelly, CP, Leffler, DA. Celiac Disease: Diagnostic Standards and Dilemmas. *Diseases.* 2015; 3: 86-101.



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## Considerations in the Use of QuantiFERON-TB Gold In-Tube (QFT-GIT) Assay

The diagnosis of latent tuberculosis infection (LTBI) is both an important clinical screening test and is often a requirement for any newly hired employees. In that arena the Interferon Gamma (IFN- $\gamma$ ) Release Assays (IGRA's) have become the “gold standard” and fueled an increase in their utilization as an alternative to the tuberculin skin test (TST).

IGRAs are blood tests that measure a T-cell response after stimulation with antigens that are specific to *Mycobacterium tuberculosis*. Although IGRAs are thought to offer improved specificity over the TST in certain populations that receive *Mycobacterium bovis* BCG vaccinations, this specificity may not be as high when testing in low-risk North-American healthcare workers and college students. It is important that variability due to preanalytical, analytical, postanalytical, manufacturing and immunological factors be minimized. A recent article in the Journal of Clinical Microbiology<sup>1</sup> deals in detail with these issues and is summarized below.

### PREANALYTICAL:

There are multiple preanalytical steps that can cause variability.

1. Disinfection of the skin is important: inadequate disinfection of the skin and rubber septums of the collection tubes can introduce microbial contaminants that may have an immunomodulatory effect, potentially causing both false positives or false negatives.
2. The order of the collection tubes is also important (starting with the nil tube and finishing with the mitogen tube) since contamination of the antigen tube with mitogen can cause a false positive and contamination of the nil tube with mitogen can cause a false negative.
3. The collected volume is also important. Studies have shown that blood volume inversely correlates with TB response in infected individuals and can result in false negatives in some individuals.
4. Excessive shaking of QFT-GIT tubes can non-specifically increase IFN- $\gamma$  response in nil or antigen tubes and lead to either a false-positive or false negative result depending on which tube is shaken excessively.
5. Delay in processing between collection and incubation can be an important source of variability with a decrease in TB response. Incubation delay has also been shown to increase the indeterminate rate.

### ANALYTICAL:

As with any laboratory test, analytical variability, even in a stable assay, can lead to dichotomous results when samples have values that are close to the assay cutoff.

Postanalytical: Manual entry can lead to clerical error resulting in false positive or negative results.

Manufacturing defects: False positive QFT-GIT results related to faulty antigen tubes have been documented a number of times. Periodic review of the positivity rate at UVMHC has been introduced to assess this issue. Indeterminate QFT-GIT results due to faulty mitogen tubes have also been reported, though not all users were affected, perhaps indicating the importance of uniform collection techniques.

(Continued from page 10)

## SYRINGE DISPOSAL

**The University of Vermont Medical Center does not accept sharps for disposal from patients!**

Chittenden Solid Waste District (CSWD) will accept needles that are packaged according to the instructions outlined in their pamphlet “GET THE POINT: Be safe with syringes and other sharps”. CSWD also has bright orange stickers to attach to a syringe container to warn handlers to be careful. These items are available at any CSWD location. You can also order them so that they are available for patients at your office 872-8111 or visit [www.cswd.net](http://www.cswd.net)

## IMMUNOLOGICAL:

A significant increase in TB response has been seen when IGRA assays follow a TST by more than 3 days. It is not clear how long this increase persists.

Important steps to minimize the variability of IGRAs:

1. Uniform disinfection of skin and tubes similar to that of blood culture.
2. Standardized tube order of draw per package insert.
3. Standardize blood volume to 1 mL.
4. Standardize gentle shaking of QFT-GIT tubes per package insert.
5. Minimize delay in processing of cells.
6. Institute a QA program to monitor positivity and indeterminate rates.
7. Draw blood samples for IGRA within 72 hrs of TST if a two-step testing system is used.

## REFERENCE

1. Banael, N, Gaur, RL, Pai, M. Interferon Gamma Release Assays for Latent Tuberculosis: What Are the Sources of Variability? *Journal of Clinical Microbiology* 54 (4): 845-850, 2016.

## LAB TOURS

Come meet the Clinical Lab Scientists and see the technology behind the lab tests you send to the University of Vermont Medical Center every day. We will be hosting laboratory tours on the second Tuesday of each month. Tours are given at the Main Pavilion at 10 am (alternate times can be arranged) and will take approximately one hour. Preregistration is required. Call (802) 847-9473 or email [LabAmbassador@UVMHealth.org](mailto:LabAmbassador@UVMHealth.org) to sign up.

**We hope to see you soon!**

## Tumor Marker Results: Cessation of Reporting of Historical Data

Quite a few years ago, when EHR, EMR, and CPOE were unfamiliar acronyms and laboratory results were primarily reported on paper, the Laboratory began manually adding historical results to tumor marker reports to facilitate interpretation. Although this step was time consuming and allowed the possibility of manual entry error, it was felt that this was worthwhile to enable easier review of results. Fast forward to the present and paper reports are by and large no longer printed and electronic health records are ubiquitous. In this setting, it no longer seems worthwhile with the potential for error to continue to enter historical results for CEA, PSA, and CA125 on the current tumor marker reports. We discontinued this practice on September 14, 2016.

However, recognizing that there is a need for a common record, for patients seen at UVMHC, but with laboratory results drawn and reported to outside hospitals, there will be the ability, on request, to have these entered into the UVMHC PRISM record. If you have any questions concerning this change please contact Dr. Greg Sharp ([gregory.sharp@uvmhealth.org](mailto:gregory.sharp@uvmhealth.org)) in the Chemistry Laboratory.

## Triglyceride Pediatric Range Change

On September 14, 2016 we began adding a comment to all Pediatric Triglyceride results stating that: "These ranges do not apply to critically ill pediatric patients on TPN." The reference ranges for these reports have caused confusion for physicians taking care of pediatric patients on TPN.

If you have any questions concerning this change please contact Dr. Greg Sharp ([gregory.sharp@uvmhealth.org](mailto:gregory.sharp@uvmhealth.org)) in the Chemistry laboratory.

## Lactic Acid Pediatric Critical Value Change

To be consistent with a recently added critical value for adult patients, a critical value for lactic acid results greater than or equal to 2.0 mmol/L will be added for Pediatric patients (age less than 18 years). This change took place on September 21, 2016.

If you have any questions concerning this change please contact Dr. Greg Sharp ([gregory.sharp@uvmhealth.org](mailto:gregory.sharp@uvmhealth.org)) in the Chemistry Laboratory.

### LABORATORY PATIENT SERVICE CENTER



**Main Campus**  
Main Pavilion, Level 2  
111 Colchester Avenue  
Burlington, VT

**Fanny Allen Campus**  
792 College Parkway  
Colchester, VT

**One South Prospect**  
1 South Prospect St  
First Floor Lobby  
Burlington, VT  
**NEW Hours: Monday - Friday 7 am to 5 pm**

**Adult Primary Care Williston**  
353 Blair Park Road  
Williston, VT  
**NEW Hours: Monday - Friday 7 am to 4 pm**

Visit [UVMHealth.org/MedCenterDrawSites](http://UVMHealth.org/MedCenterDrawSites) for patient service center hours and special test considerations.

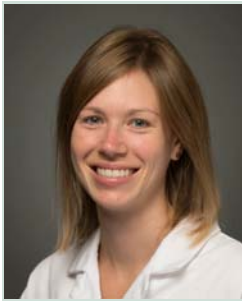
All UVM Medical Center phlebotomists are nationally certified

### GET TEST RESULTS ONLINE!

MyHealth Online

Did you know that your patients can get their UVM Medical Center test results online by signing up for a MyHealth Online account?

To sign up visit: [UVMHealth.org/MedCenterMyHealth](http://UVMHealth.org/MedCenterMyHealth)



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## New Test: Group B Strep PCR for Penicillin Allergy

Group B Streptococcus (GBS), *Streptococcus agalactiae*, is a cause of morbidity and mortality among infants. Maternal vaginal or rectal colonization with GBS is a risk factor for disease in infants. Up to 10-30% of pregnant women are vaginally or rectally colonized with GBS and may transmit the organism to their infant during delivery. The Centers for Disease Control and Prevention recommends screening for colonization with GBS at 35 to 37 weeks gestation as a guide for intrapartum antibiotic prophylaxis to decrease the risk of infection with GBS in infants. First line therapy for intrapartum antibiotics prophylaxis is penicillin.

GBS is best detected by molecular based methods such as PCR. Molecular detection of GBS is significantly more sensitive (90%-97%) than compared to antepartum culture (58%-84%). For this reason, pregnant women should undergo PCR based screening for GBS. Effective 10/26/2016 please order GROUP B STREP, PCR (Test Code SXBBD) for GBS screening in pregnant women without a penicillin allergy.

Culture is performed only for GBS positive pregnant women who have a penicillin allergy and require additional susceptibility information for other antibiotics. To simplify the ordering process, we are eliminating the GBS culture option and replacing it with a test named “Group B Strep PCR for Penicillin Allergy” This test will screen

for GBS via PCR and then reflex to culture with sensitivities if GBS is positive. This test should only be ordered for pregnant women that have a penicillin allergy.

Group B Strep PCR for Penicillin Allergy	
SQ Test Code:	SXBPEN
Mayo Access ID:	FAH5720
Lab Division:	Microbiology 1
CPT Code(s):	87653
Method	PCR
Instrumentation:	BD Max
Sample Requirements:	Use a Bacterial Collection Kit to collect a vaginal and rectal sample, refrigerate after collection.
Test Note:	This test is intended for pregnant women with a penicillin allergy. A PCR test for Group B Strep will be performed. If the test is positive, a culture will also be done to provide additional susceptibility information. It is possible to have a positive PCR result and not grow the organism in culture because PCR has a higher sensitivity and is able to detect Group B Strep in lower numbers. <i>If this test is positive a Bacterial Culture will be performed</i> <u><a href="#">See Laboratory Reflex Policy.</a></u>
Expected Value:	Negative
Days Performed:	Monday—Friday
Analytical Time::	2 days
Is the test available STAT?	No
New York State Certified?	Yes
Effective Date:	October 26, 2016
Test Catalog information is <u><a href="#">available here.</a></u>	



## REFERENCES FOR GROUP B PCR

1. Prevention of Perinatal Group B Streptococcal Disease: Revised Guidelines from CDC, Recommendations and Reports, Morbidity and Mortality Weekly Report (MMWR) 2010 Nov 19; 59(RR10);1-32 [http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5910a1.htm?s\\_cid=rr5910a1\\_w](http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5910a1.htm?s_cid=rr5910a1_w)
2. York MK, Hillier SL, Church DL: Group B Streptococcus Cultures. In Clinical Microbiology Procedures Handbook. Edited by LS Garcia. Washington DC, American Society for Microbiology, 2010, section 3.9.2
3. Davies HD, Miller MA, Faro S, et. al. Multicenter study of a rapid molecular-based assay for the diagnosis of group B Streptococcus colonization in pregnant women. Clin Infect Dis. 2004 Oct 15;39(8):1129-35.

## Bacterial Culture Test Inactivation

Effective September 14, 2016 the option of Bacterial Culture was inactivated. The appropriate test to order is Bacterial Culture/Smear (Test Code: RCS, PRISM Code: LAB2523, Mayo Access ID: FAH5295).

The best specimens for culture are tissue, fluids, aspirates, or curettings. In the absence of those specimens, it is essential to have the benefit of information from a Gram smear. The Bacterial (white capped vial) Flocked swab collection device allows for ample material to perform both gram smear and culture .

The diagnosis of bacterial infections requires documentation of both an inflammatory response (host response) and the presence of an etiologic bacteriologic agent. The Gram smear serves as a guarantor that the quality of the specimen is good because there is an associated inflammatory response. Without this information it is often difficult or impossible to determine the significance of the culture, particularly if multiple organisms have been isolated and the specimen is from a site that could be contaminated by indigenous flora. We do not routinely evaluate cultures with mixed organisms if a Gram smear is not available. In addition, the Gram smear may serve as a clue that bacteria are present, but have not been isolated in culture. The most common situation is the presence of anaerobic bacteria on the smear if an anaerobic culture was not ordered.

### REMINDER: DIRTY URINE FOR STD'S



#### URINE COLLECTION FOR CHLAMYDIA/GC FOR MALE AND FEMALE

Collecting a dirty urine sample for STD's is not anything like a clean catch collection.

The area should not be cleansed and the first stream of 20 -30 mL of urine should be collected in a sterile container, the rest should be voided into the toilet.

**A larger volume of urine may result in a rRNA target dilution that may reduce sensitivity and the sample will be rejected.**

If the patient also needs to have a bacterial urine culture collected, that will require a separate collection.

#### INSTRUCTIONS FOR COLLECTING A DIRTY URINE

- Have patient wash hands with soap and water, rinse and dry.
- First voided urine is required. Patient should not have urinated for at least 1 hour prior to urine collection.
- **Do not cleanse** area prior to collection.
- Use a pen or marker and draw a line at the 30 mL mark on the outside of the urine collection container. Use the measurement scale on the side of the container.
- Specimen collection volume must be **less than 2 tablespoons** (30 mL), if more urine is collected specimen will need to be recollected. If more urine is voided **do not** pour off urine to the 30 mL mark, collect a sample at another time.
- The sample must be refrigerated or stored in a cooler with ice after collection and transported to the lab within 24-hours.

## Compliance News

### HEMACHROMATOSIS GENETIC TESTING:

Effective July 1, 2016, **Medicaid** added Hemachromatosis Genetic Testing as a covered service.

**This test does require Prior Authorization.**

### BC/BS OF VERMONT CHANGES

Effective 10/1/16- Morphometric analysis; nerve (CPT 88356) requires prior authorization.

Effective 9/1/16- MTHFR (5,10-methylenetetrahydrofolate reductase) CPT 81291 is considered “investigational” and will no longer be covered by BCBSVT. If ordering this test, please obtain the Commercial: Advance Notice of Potential Non-Coverage form and submit with the requisition to the laboratory.

## Zika Testing Continued from page 1

- A pregnant woman WITH or WITHOUT symptoms\* who had a history of travel to an area with active Zika transmission within the previous 12 weeks, OR
- A pregnant woman who had unprotected sexual exposure to semen of a man\*\* who had previously traveled to an area with active Zika

\*Symptoms consistent with Zika virus include acute febrile illness, rash, arthralgia, conjunctivitis, myalgia or headache

\*\*Man does NOT need to be a confirmed Zika virus case

*NOTE: Current CDC research suggests that Guillain-Barre Syndrome (GBS) is strongly associated with Zika; however, only a small proportion of people with recent Zika virus infection get GBS. If you have a patient with a GBS diagnosis and a recent travel history to an area with active Zika transmission, call the VT Department of Health at (802) 863-7240 for further guidance on specimen collection for Zika lab testing.*

**Testing will not be approved for asymptomatic women considering pregnancy.**

**The current CDC recommendation is for women to wait 8 weeks after return from travel to attempt conception.**

### SAMPLE INFORMATION

Container	Specimen	Temperature	Collect Vol	Submit Vol	Minimum Volume
SST	Serum	Refrigerate	4 mL	1 mL	1 mL
Sterile Container	Urine	Refrigerate	2 mL	2 mL	1 mL

It is recommended to send both Serum AND Urine at the same time. There are two test options – PCR and Elisa. VDH will determine which test to perform based on the information provided to Epidemiology.

Other useful documents:

[CDC's Response to Zika. What happens when I am tested for Zika and when will I get my results?](#)

[VDH Laboratory Specimen Collection for Zika virus](#)

[VDH Clinical Test Request Form](#)

[Zika Virus Testing](#) in our test catalog



111 Colchester Avenue  
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**PATHOLOGY & LABORATORY MEDICINE COMMUNIQUÉ — OCTOBER 2016**

**PATHOLOGY & LABORATORY MEDICINE COMMUNIQUÉ**

**NEWSLETTER EDITORS**

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(802) 847-5905

**WEBSITE**

[UVMLabs.TestCatalog.org/](http://UVMLabs.TestCatalog.org/)

## Thanksgiving Holiday

### Laboratory Hours

Laboratory Collection Site	Thursday 11/24/2016 Thanksgiving Day	Friday 11/25/2016
Main Campus	Closed	7 am - 5 pm
Fanny Allen Campus	Closed	6:30 am - 5 pm
One South Prospect	Closed	7 am - 4 pm
Blair Park	Closed	7 am - 4 pm

Please stop at patient registration before proceeding to the Laboratory. Patients are seen in the order in which they arrive, unless they need immediate testing, timed tests, or have special needs. Some testing must be scheduled in advance or have other special considerations.