ACL Laboratories
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Test Bulletin

August 2018

Cyclospora Outbreak

In recent weeks there have been numerous outbreaks of *Cyclospora* infections due to contaminated salads from McDonald's fast-food chain restaurants, as well as other foods. The Center for Disease Control (CDC) has been providing updates. *Cyclospora cayetanensis* is a single-celled parasite that causes an intestinal infection called cyclosporiasis. People that have contracted *Cyclospora* may not experience symptoms, such as watery diarrhea, until about one week after having eaten contaminated food. Patients with symptoms should seek medical treatment.

Cyclospora is a difficult organism to visualize on a traditional ova and parasite examination. In the event that *Cyclospora* infection is suspected, the most appropriate test to order is CYCS Cyclospora/Cystoisospora Screen (Test Order Code CYCS). Please note, only *Cyclospora* and *Cystoisospora* will be detected with this test. If other pathogens are included in the differential diagnosis, specific tests for those pathogens should also be ordered. Trimethoprim/sulfamethoxazole (TMP/SMX) is the usual therapy for *Cyclospora* infection.

ACL Announces New Test NT proBNP (Test Order Code NTPBNP)

Effective Wednesday, August 15, 2018, ACL Laboratories will convert natriuretic peptide testing from BNP (B-type natriuretic peptide) to NT proBNP (N-terminal pro b-type natriuretic peptide). BNP will be discontinued in favor of NT proBNP testing.

B-type natriuretic peptide (BNP) and NT proBNP are two different cardiac biomarkers with different characteristics that have been used in the diagnosis, prognosis, and management of heart failure. Recent clinical evidence suggests that NT proBNP is a superior marker of heart failure compared to BNP. The advantages of NT proBNP include greater sensitivity for the detection of chronic heart failure in patients with preserved left ventricular ejection fraction (LVEF). NT proBNP has also been used in the risk stratification of patients with acute coronary syndrome and as an aid in the assessment of increased risk of cardiovascular events and mortality in patients at risk for heart failure who have stable coronary artery disease.

The rise of NT proBNP levels in response to myocardial stress is often several orders of magnitude higher than BNP. In addition, half-life is increased (NT proBNP is ~120 minutes vs 20 minutes for BNP). All of this contributes to greater analytical stability, accuracy, and precision. Also, because of these factors, NT proBNP has a different reference range than BNP.

One major clinical advantage of NT proBNP is that levels are NOT affected by current heart failure treatment regimens including Entresto.

Although both markers may be affected by renal dysfunction, NT proBNP is cleared essentially by the kidneys while BNP may also be cleared through BNP receptors. This difference in elimination routes helps explain the differences in reference ranges, especially in patients > 75 years of age.

Table of Contents

Cyclospora Outbreak – **1**
ACL Announces New Test NT proBNP (Test Order Code NTPBNP) – **1**
Prenatal Maternal Serum Aneuploidy Screening Updates – **3**
ACL Announces New Test, Testosterone Free and Total, Bioavailable & SHBG, Male (Test Order Code TSTFPB) – **4**
Potential Sulfasalazine Interference with Routine Chemistry Tests – **5**
ACL Laboratories Discontinues Campylobacter Antigen Test (Test Order Code CAMPAG) – **5**
ACL Laboratories Discontinues Quantitative Duodenal Aspirate (Test Order Code QDAC) and Quantitative Tissue (Test Order Code QTIS) Culture Test Order Codes – **6**
Carbamazepine, Free and Total (Test Order Code CARBFT) – **6**
Carbamazepine and Metabolite (Test Order Code CARBME) – **7**
Valproic Acid, Free and Total (Test Order Code VPAFT) – **7**
Inactivated Codes with New Orderable Replacement Codes – **8**
Inactivated Codes with REF Codes – **8**

Results obtained from NT proBNP and BNP are NOT equivalent and blood concentrations vary significantly between the two assays. Therefore, results obtained from NT pro BNP and BNP cannot be compared or interchanged.

	B-Natriuretic Peptide (Current Test)	NT proBNP (New Test – Effective Wednesday, August 15, 2018)
Test Order Code	BNPEP	NTPBNP
Reference Range	<100 pg/mL (all ages)	<75 years: <126 pg/mL ≥75 years: <451 pg/mL
Sample Stability	EDTA Plasma	Lithium Heparin Plasma
Sample Type	Room Temperature: 4 hours Refrigerated: 7 hours Frozen: 14 days	Room Temperature: 3 days Refrigerated: 3 days Frozen: 14 days

Effective Wednesday, August 15, 2018, NT proBNP (Test Order Code NTBNP), currently sent to Cleveland Clinic Laboratories, will be **inactivated** as the test will now be performed by ACL Laboratories. The reference range for NT proBNP remains unchanged.

For additional information regarding this test, as well as specimen collection requirements, please contact ACL Client Services at 1.800.877.7016 or visit our website at www.acllaboratories.com/test-catalog/.

References:

Lin DC, Diamandis EP, Januzzi JL, Maisel A, Jaffe AS, Clerico A. Natriuretic peptides in heart failure. *Clin Chem*. 60(8): 1040-6, 2014.

Chow SL, Maisel AS, Anand I, Bozkurt B, de Boer RA, Felker M, Fonarow GC, Greenberg B, Januzzi JL, Kiernan MS, Liu PP, Wang TJ, Yancy CW, Zile MR, et al. Role of Biomarkers for the Prevention, Assessment, and Management of Heart Failure: A Scientific Statement From the American Heart Association. *Circulation* 135(22), 2017.

Wettersten N, Maisel AS. Biomarkers for heart failure: an update for practitioners of internal medicine. *Am J Med*. 129(6): 560-7, 2016.

McKie PM, Burnett Jr JC NT-proBNP: The Gold Standard Biomarker in Heart Failure. *J Am Coll Cardiol*. 68:2437-9, 2016.

Prenatal Maternal Serum Aneuploidy Screening Updates

Effective Wednesday, August 15, 2018, ACL Laboratories will discontinue the following maternal serum screening Test Order Codes: REF787, REF788, REF789, TMS, and PENTA. Comparable replacement test order codes are available, as summarized below.

Discontinued *Effective Wednesday, August 15, 2018*			Recommended Replacement		
Test Name	**Test Order Code**	**Performing Laboratory**	**Test Name**	**Test Order Code**	**Performing Laboratory**
Maternal Serum Screen, First Trimester	REF787 (previously MSSSFR)	ARUP	First Trimester Prenatal Screen	FTPSCN	Eurofins NTD
Maternal Screening, Sequential, Specimen #1	REF788 (previously MSSS1R)	ARUP	First Trimester Prenatal Screen	FTPSCN	Eurofins NTD
Maternal Screening, Sequential, Specimen #2	REF789 (previously MSSS2R)	ARUP	Sequential Screen NTD	STSSEQ	Eurofins NTD
Triple Marker Screen, Maternal	TMS	ACL Laboratories	Quad Marker Screen, Maternal	QMS	ACL Laboratories
Penta Maternal Screen	PENTA	Quest Diagnostics	Quad Marker Screen, Maternal	QMS	ACL Laboratories

In comparison to the screenings performed at ARUP, first trimester and sequential screening at Eurofins NTD provide superior test performance and clinician- and patient-friendly report interpretation. First trimester screening at NTD utilizes three biochemical markers, free beta hCG, pregnancy-associated plasma protein A (PAPP-A), and alpha fetoprotein, in combination with biophysical markers, including nuchal translucency (NT) measurement and fetal nasal bone assessment, to provide detection rates of 93-96% and 95% for trisomy 21 and trisomies 18/13, respectively. NTD also offers the option of sequential screening, which measures the levels of four pregnancy-related analytes, with detection rates of 95% for trisomies 21 and 18, and 90% for open spina bifida.

Reference: www.ntdlabs.com/maternal-marker-testing/, ltd.aruplab.com/Tests/Pdf/311

Based on these new testing recommendations, expect the following changes to work-flow for first trimester screening:

- Eurofins NTD supplies test requisitions specific for maternal serum screening
- Rather than a peripheral blood sample, analyte analysis at Eurofins NTD is performed from maternal blood spots collected on filter paper, which is attached to the test requisition form

ACL's quad marker screen provides superior performance in comparison to the triple marker screen offered by ACL and comparable performance to the penta maternal screen offered by Quest Diagnostics. The quad marker screen utilizes four biochemical markers to provide detection rates of 81% for trisomy 21 and 80% for trisomy 18 and open spina bifida.

For these second trimester screening test changes, there are **NO** changes in specimen processing and handling.

If you have any questions, please consult the ACL Laboratories Directory of Services at https://www.acllaboratories.com/test-catalog/ or contact ACL's genetic counselors at 847.349.7440.

ACL Announces New Test, Testosterone Free and Total, Bioavailable & SHBG, Male (Test Order Code TSTFPB)

Effective Wednesday, August 15, 2018, ACL Laboratories will offer a new Test, Testosterone Free and Total, Bioavailable & SHBG, Male (Test Order Code TSTFPB). This test combines two current send-out tests into one test that ACL Laboratories will perform.

This test is intended for adult males only. It is useful for the evaluation of suspected hypogonadism in men. Free and bioavailable testosterone levels more accurately reflect true androgen status than total testosterone levels.

This test includes the following components:

- Testosterone, Total
- Sex Hormone Binding Globulin
- Testosterone, Free (Calculated)
- Testosterone, % Free (Calculated)
- Testosterone, Bioavailable (Calculated)

Testosterone, Total and Sex Hormone Binding Globulin (Test Order Code SHBG) are measured parameters. Free Testosterone, and Bioavailable Testosterone are calculated parameters derived from mathematical equations based on constants for the binding of testosterone to albumin and/or sex hormone binding globulin. (Vermeulen A, Verdonck L, Kaufman JM. A critical evaluation of simple methods for the estimation of free testosterone in serum. *J Clin Endocrinol Metab*. 84:3666-3672, 1999)

Specimen Requirements:
Preferred specimen collection is between 6 am and 10 am
Collect one gold gel 3.5 mL tube
Transport refrigerated

Test Availability:
Testing is performed daily
Results available within 24 hours

New Reference Ranges:

Description	Male Age	Reference Range
Free Testosterone	< 15 years	No reference range
	15 to 17 years	20 – 173 pg/mL
	18 years and older	47 – 244 pg/mL
Testosterone, % Free	< 15 years	No reference range
	15 years and older	1.6 – 2.9%
Testosterone, Bioavailable	< 15 years	No reference range
	15 to 17 years	20 – 509 ng/dL
	18 years and older	131 – 682 ng/dL

For females and children (including males less than 15 years old), refer to the following tests:

- Testosterone, Free & Total (Includes Sex Hormone Binding Globulin), Female or Children (Test Order Code TSTFFR)
- Testosterone, Bioavailable & Sex Hormone Binding Globulin (w/Total Testost), Females or Children (Test Order Code TSSHFR)

Effective Wednesday, August 15, 2018, the following tests will **no longer be offered:**

- Testosterone, Bioavailable & SHBG (w/Total Testosterone), Adult Male. (Test Order Code TSSHMR)
- Testosterone, Free and Total (includes Sex Hormone Binding Globulin), Adult Male, (Test Order Code TSTFMR)

For additional information regarding these tests, as well as specimen collection requirements, please contact ACL Client Services at 1.800.877.7016 or visit our website at www.acllaboratories.com/test-catalog/.

Potential Sulfasalazine Interference with Routine Chemistry Tests

Sulfasalazine is routinely used in the treatment of inflammatory bowel disease, ulcerative colitis, Crohn's disease and rheumatoid arthritis. ACL's chemistry instrumentation vendor has informed ACL that this drug may interfere with the detection system used for Ammonia causing falsely elevated concentrations (<10% – 66%) or falsely decreased Alanine Aminotransferase (ALT) concentrations (29 – 72%). This interference was observed at extremely high and toxic concentrations of sulfasalazine.

To minimize this potential interference, it is recommended that venipuncture occur ***before*** administration of sulfasalazine. Additionally, Providers need to be aware of this potential source of interference, especially if laboratory results are inconsistent with the patient clinical presentation.

From time to time ACL is made aware of interfering substances that may impact chemistry testing results. Manufacturers regularly provide updated Instructions for Use (IFU). These contain reference information with respect to assay performance and potential interferences. These documents are retained by the laboratory and will be used as a reference for any questions or concerns that may arise.

Please direct any questions or concerns to:
Ken Copeland, PhD
Technical Director, Chemistry
Kenneth.Copeland@aurora.org

ACL Laboratories Discontinues Campylobacter Antigen Test (Test Order Code CAMPAG)

Effective Wednesday, August 15, 2018, ACL Laboratories will no longer offer the *Campylobacter* Antigen Test (Test Order Code CAMPAG). This test is an immunochromatographic test to detect *Campylobacter* antigens and is rarely used and not recommended because it is known to have a high rate of false positivity and requires confirmatory testing. ACL will continue to offer the following tests, which are more accurate and do not require confirmatory testing, in the event that *Campylobacter* gastroenteritis is suspected:

Gastrointestinal Pathogen Panel (Test Order Code GPPNL) – a molecular test that detects 13 common bacterial, viral, and parasitic causes of infectious gastroenteritis including *Campylobacter*. **(Patients will need to verify with their insurance company, as this test may require prior authorization.)**

Culture, Enteric Pathogen (Test Order Code ENPC) – utilizes culture and enzyme immunoassay to detect common causes of bacterial gastroenteritis. *Campylobacter* antigens are detected by enzyme immunoassay.

ACL Laboratories Discontinues Quantitative Duodenal Aspirate (Test Order Code QDAC) and Quantitative Tissue (Test Order Code QTIS) Culture Test Order Codes

Effective Wednesday, August 15, 2018, ACL Laboratories will discontinue offering Quantitative Duodenal Aspirate Culture test (Test Order Code QDAC) and Quantitative Tissue Culture test (Test Order Code QTIS) due to extremely low volumes. The Quantitative Duodenal Aspirate Culture is primarily utilized to determine the presence of abnormal bacterial overgrowth in the duodenum of the small intestine, but does not identify the organisms present. The Quantitative Tissue Culture is sometimes utilized to assess wound healing and simply provides colony counts, but no susceptibility testing results. For this reason, traditional wound cultures, which include susceptibility testing results, are often of greater value.

In the event a Provider requires these tests to be performed, a miscellaneous laboratory test order would be required with a notation that indicates a Quantitative Duodenal Aspirate culture or Quantitative Tissue Culture needs to be performed. The specimens will be sent to a reference laboratory for testing.

For additional information regarding these tests, please contact ACL Client Services at 1.800.877.7016.

Carbamazepine, Free and Total (Test Order Code CARBFT)

Effective Tuesday, August 28, 2018, Cleveland Clinic Laboratories (CCL), the performing laboratory, will update the specimen requirements and test performance for Carbamazepine, Free and Total (Test Order Code CARBFT).

Specimen collection requirements are as follows:

Carbamazepine, Free and Total (Test Order Code CARBFT)	Current Specimen Collection Requirements	New Specimen Collection Requirement – *Effective Tuesday, August 28, 2018*
Collect	One light green (lithium heparin gel) 4.5 mL (also acceptable: Two green (sodium or lithium heparin) 2.0 mL and gold gel 5.0 mL)	One plain red 6.0 mL
Transport	3.0 mL (min: 1.8 mL) plasma or serum frozen	3.0 mL (min: 2.0 mL) serum frozen
Unacceptable Conditions	None	Gel separator tubes
Stability	Ambient: 8 Hours after separation from cells Refrigerated: 48 Hours after separation from cells Frozen: Longer periods after separation from cells	Ambient: 2 Days after separation from cells Refrigerated: 7 Days after separation from cells Frozen: 14 Days after separation from cells

Carbamazepine and Metabolite (Test Order Code CARBME)

Effective immediately, Cleveland Clinic Laboratories (CCL), the performing laboratory, updated the specimen requirements for Carbamazepine and Metabolite (Test Order Code CARBME).

Specimen collection requirements are as follows:

Carbamazepine and Metabolite (CARBME)	Current Specimen Collection Requirements	New Specimen Collection Requirement – *Effective Immediately*
Collect	One light green (lithium heparin gel) 4.5 mL (also acceptable: green (lithium heparin no gel) 6.0 mL and green (sodium heparin no gel) 6.0 mL)	One green (lithium heparin no gel) 4.5 mL (also acceptable: green (sodium heparin no gel) 6.0 mL and plain red 4.0 mL). Collect immediately prior to next dose.
Transport	3.0 mL (min: 0.4 mL) plasma refrigerated	3.0 mL (min: 1.0 mL) plasma or serum refrigerated
Unacceptable Conditions	None	Gel separator tubes
Stability	Ambient: 8 Hours after separation from cells Refrigerated: 2 Days after separation from cells Frozen: 1 Month at -20°C, after separation from cells	Ambient: Unacceptable Refrigerated: 1 Week after separation from cells Frozen: 1 Month at -20°C, after separation from cells
Performed	Friday	Weekdays
Reporting Time	Final within 9 Days	Final within 5 Days

Valproic Acid, Free and Total (Test Order Code VPAFT)

Effective Tuesday, August 28, 2018, Cleveland Clinic Laboratories (CCL), the performing laboratory, will update the specimen requirements and test performance for Valproic Acid, Free and Total (Test Order Code VPAFT).

Specimen collection requirements are as follows:

Valproic Acid, Free and Total (Test Order Code VPAFT)	Current Specimen Collection Requirements	New Specimen Collection Requirement – *Effective Tuesday, August 28, 2018*
Collect	One green (sodium or lithium heparin) 6.0 mL Collect immediately before next dose.	One plain red 6.0 mL Collect immediately before next dose.
Transport	3.0 mL (min: 1.8 mL) plasma refrigerated	3.0 mL (min: 1.8 mL) serum refrigerated
Unacceptable Conditions	None	Gel separator tubes
Stability	Ambient: 1 Day Refrigerated: 1 Week Frozen: 1 Month	Ambient: Unacceptable Refrigerated: 5 Days after separation from cells Frozen: 14 Days after separation from cells

Inactivated Codes with New Orderable Replacement Codes

Inactivated Test Name	Inactivated Test Order Codes	Recommended Alternate Test Name	Recommended Alternate Test Order Code
Aquaporin-4 Receptor Antibody, IgG by IFA with Reflex to Titer, Serum	REF786	Aquaporin-4 Receptor Antibody, IgG by IFA with Reflex to Titer	AQUA4 (w/reflex to AQUTTR)
Platelet Autoantibodies	PLABBC	Platelet Autoantibodies Profile	PLATPR
Platelet Autoantibodies Profile, Whole Blood	REF784	Platelet Autoantibodies Profile	PLATPR
Nucleophosmin (NPM1) Mutation Analysis	REF782	Nucleophosmin (NPM1) Mutation Analysis	NPM1MT
Cytomegalovirus Antiviral Drug Resistance	CYTOSQ	Cytomegalovirus Antiviral Drug Resistance	CMVRSS

Inactivated Codes with REF Codes

Inactivated Test Name	Inactivated Test Order Codes	Reference Laboratory & Test Order Code/Number	Alternate Test Name
Echovirus Antibodies	ECHOV	Quest SJC (35139X)	Echovirus Antibody Panel