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CHANGES TO MATERNAL SERUM SCREEN TEST ORDER REQUISITIONS AND RISK CALCULATION ALGORITHM

ANNU KHAJURIA, PHD, FCACB, FACB, DIVISION OF LABORATORY MEDICINE

Effective September 24th, 2012, several changes will take effect for Maternal Serum Screen (MSS) test order requisitions and the risk calculation algorithm to conform to recommendations by the College of American Pathologist (CAP).

TEST

Maternal serum screening measures analytes produced by the fetus and placenta. It has become a standard tool in obstetrical care to identify pregnancies that are at higher risk for Down syndrome, open spina bifida (OSB) and trisomy 18. The analyte values, as multiples of the median (MoMs) for a given gestational age, and maternal demographics are used together in a mathematical model to derive risk estimates. Marshfield Labs offers second trimester maternal serum screening between 15 and 21 weeks gestational age. A positive screen is not a definitive diagnosis but recommends further evaluation.

The test panels offered are:
AFP-1: a maternal serum single marker screen for risk assessment of OSB only.
AFP-4: a quadruple maternal serum screen (QUAD) measuring four analytes for risk assessment of OSB, trisomy 21 (Down syndrome) and trisomy 18.

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TEST ORDER REQUISITION CHANGES

Correct test ordering practices are critical to minimize the chance of incorrect risk assessment and thereby inappropriate management. The following changes are designed to minimize errors occurring during test ordering.

1. Test descriptions for test code AFP-1 and AFP-4 are updated as:
   AFP1 (single marker MSS)
   Second trimester MSS for open spina bifida only (between 15 wks, 0 days and 21 wks, 6 days).
   AFP4 (quadruple MSS)
   Second trimester MSS for open spina bifida defect, Down syndrome and trisomy 18 (between 15 wks, 0 day and 21 wks, 6 days). "Not intended for patients who already have had a first trimester screen. Consider AFP1 instead".
2. Clinical Information section of test requisition will have the following updates:
   Has the patient had a first trimester screen:
   If yes, order AFP1 (Single marker MSS)
3. Cigarette smoker status has been added in the clinical information section of the test requisition. Smokers have been shown to have a higher screen positive rate for Down syndrome and trisomy 18. Second trimester QUAD tests show reduced MoM for hGC and uE3 and increased MoM for AFP and inhibin A. Adjustment for smoking in risk assessment calculations will help avoid false screen positive results and unnecessary subsequent invasive testing.

RISK CALCULATION ALGORITHM CHANGES

In order to compute reliable risks for OSB and Down syndrome, sets of published parameters are used that mathematically model the multidimensional relationship between markers in affected and unaffected pregnancies. The proposed algorithms are Wald 2000, Haddow 98 and SURUSS 2003. Presently, Marshfield Lab uses Benetech PRA software to calculate the risk estimation using the Wald 2000 algorithm. New guidelines recommend changing from Wald 2000 to SURUSS 2003 to improve both the detection rate and false positive rate in Down syndrome. An in-house comparison using 40 patients showed a 25% decrease in false positive results by using the SURUSS algorithm.

Second trimester QUAD screen performance characteristics are given in the table below. The SURUSS study data was derived from 47,000 singleton pregnancies of which 101 had Down syndrome. Currently, the SURUSS model provides the best overall MSS performance characteristics.

RISK CUT-OFF AT MID-TRIMESTER			
1 IN 270 [WALD 2000]		1 IN 300 [SURUSS 2003]	
DETECTION RATE %	FALSE POSITIVE RATE %	DETECTION RATE %	FALSE POSITIVE RATE %
79 (LMP) 82 (US)	8.2 (LMP) 6.8 (US)	86 AT FIXED 85	6.6 6.2

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The new risk cut-off for Down syndrome will be 1/300 vs. 1/295 at mid-trimester. The risk cutoffs for OSB and trisomy 18 will, however, remain unchanged as 1/243 at 2.5 MoM for AFP and 1/100 at mid-trimester, respectively.

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- Wald NL, Rodeck C, Hackshaw AK and Rudnicka A. SURUSS in perspective. Seminars in Perinatology 2005; 29: 225-235.
- Wald NJ, Hackshaw AK and Cuckle HS. Maternal serum alpha-fetoprotein screening for open tube defects: Revised statistical parameters. BJOG 2000; 107: 295-298.
- Zhang J, Lambert-Messerlian G, Palomaki GE and Canick JA. Impact of smoking on maternal serum markers screening in the first and second trimester. Prenatal Diagnosis 2011; 31: 583-588.

For any questions and additional information, call 715-221-6700 or 800-222-5835 and ask for: Annu Khajuria, PhD, FACAB, FACB.

CHANGES IN THE VANCOMYCIN THERAPEUTIC REFERENCE RANGE

THOMAS FRITSCHE MD, PHD, FCAP AND ANNU KHAJURIA, PHD, FCACB, FACB, DIVISION OF LABORATORY MEDICINE

Effective September 24th, 2012, the following changes will be made to the reportable vancomycin reference ranges to conform with recommendations from the American Society of Health-System Pharmacists and the Infectious Diseases Society of America.

Vancomycin is a systemic antimicrobial agent widely used for the treatment of gram-positive infections including serious infections involving methicillin–resistant *Staphylococcus aureus* (MRSA). Recommendations from the American Society of Health-System Pharmacists, the Infectious Diseases Society of America and Society of Infectious Diseases Pharmacists state that trough serum vancomycin concentrations are the single most accurate and effective method for monitoring vancomycin levels. Trough levels should be obtained just before the fourth dose in patients with normal renal function. Optimal therapy requires trough levels to be maintained at 10-15 µg/ml and evidence does not support the monitoring of peak concentrations to decrease the frequency of nephrotoxicity.

THE NEW THERAPEUTIC REFERENCE RANGE FOR VANCOMYCIN TROUGH CONCENTRATIONS WILL BE:

Therapeutic concentrations:	10 – 15 µg/mL
Serious Infections:	15 – 20 µg/mL
Call back:	>30 µg/mL
Toxic levels:	≥80 µg/mL

- Vancomycin trough concentrations should always be maintained at ≥10 µg/mL to avoid the development of resistance.
- For serious *Staphylococcus aureus* infections such as septicemia, infective endocarditis, osteomyelitis,

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meningitis, pneumonia and severe Skin and Soft Tissue Infections (SSTI) (necrotizing fasciitis), vancomycin trough concentrations of **15-20 µg/mL are recommended**.

- Vancomycin-induced nephrotoxicity is indicated if an increase in serum creatinine of 0.5 mg/dL or a 50% increase from baseline (whichever is greater) is observed following several days of therapy in the absence of an alternative explanation. A minimum of two or three consecutive serum creatinine concentrations should be submitted during the course of therapy to monitor for possible nephrotoxicity.

REFERENCES

- Rybak M, Lomaestro B, Rotschafer JC, et al. Therapeutic drug monitoring of vancomycin in adult patients: A consensus review of the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, and the Society of Infectious Diseases Pharmacists. Am J Health Syst Pharm 2009; 66:82-98.
- Clinical Practice Guidelines by the Infectious Diseases Society for the Treatment of Methicillin-Resistant *Staphylococcus aureus* Infections in Adults and Children. Clinical Infectious Diseases 2011; 52(3):e18-e55.

For questions and additional information, please call 715-221-6700 or 800-222-5835 and ask for either:
Thomas Fritsche, MD, PhD, FCAP
Annu Khajuria, PhD, FCACB, FACB

THE DO'S AND DON'T'S OF BORDETELLA PERTUSSIS PCR TESTING

TIMOTHY UPHOFF, PHD, DABMG, MLS(ASCP)CM

As the start of another fall season approaches Marshfield Labs continues to see high volumes of samples submitted for Bordetella pertussis (whooping cough) testing. From January 1, 2012 through July 31, 2012, 3,496 cases (2,498 confirmed and 998 probable) of pertussis with completed investigations have been reported among Wisconsin residents. During the past nine months, Marshfield Labs has received about 10 times the number of samples submitted as compared with the same time period during the previous year. Since this outbreak began, Marshfield Labs has been performing PCR tests for *B. pertussis* and *B. parapertussis* seven days per week.

While bacterial culture is nearly 100% specific, its poor sensitivity (60%) in comparison with PCR testing (90-99%) makes culture less useful for diagnosing pertussis especially in adults and in the later stages of the disease. Bacterial culture for *B. pertussis* and *B. parapertussis* is not routinely recommended or available from Marshfield Labs.

DO follow the Wisconsin Division of Public Health Communicable Disease Surveillance Guidelines for Pertussis: http://www.dhs.wisconsin.gov/communicable/EpiNetGuidance/EpiPertussis.pdf

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DO test all symptomatic or probable cases suspected of having pertussis:

The CDC Pertussis clinical case definition is as follows: a cough illness lasting at least 2 weeks with one of the following: paroxysms of coughing, inspiratory "whoop," or post-tussive vomiting, without other apparent cause (as reported by a health professional).

DO NOT test asymptomatic individuals:

The CDC recommends only patients with signs and symptoms consistent with pertussis should be tested by PCR to confirm the diagnosis. Testing asymptomatic persons should be avoided as it increases the likelihood of obtaining falsely-positive results. Asymptomatic close contacts of confirmed cases should not be tested and testing of contacts should not be used for post-exposure prophylaxis decisions.

DO NOT engage in practices that may lead to potential false positive results:

Because of the high sensitivity of PCR tests, clinicians should be careful to avoid potential contamination of environmental surfaces and patient specimens with *B. pertussis* DNA either from other clinical specimens or vaccine components. Unlike culture, PCR does not require viable (live) bacteria present in the specimen. Pseudo–outbreaks of pertussis have been linked to both types of contamination (Loeffelholz, 2012; Mandal, Tatti et al., 2012).

- Wear gloves immediately before and during specimen collection or vaccine preparation and administration with immediate disposal of gloves after the procedure.
- Clean clinic surfaces using a 10% bleach solution to reduce the amount of nucleic acids in the clinic environment.
- Prepare and administer vaccines in areas separate from pertussis specimen collection areas; this may reduce the opportunity for cross contamination of clinical specimens.
- Take care when preparing and administering pertussis vaccines to avoid contamination of surfaces with vaccine.
- Vaccines shown to contain PCR-detectable DNA include Pentacel®, Daptacel®, and Adacel® (Leber A et al., 2010). If health care professionals adhere to good practices, there is no need to switch vaccines.

DO interpret Bordetella PCR results in conjunction with the clinical symptoms and epidemiological information:

- PCR has optimal sensitivity during the first 3 weeks of cough when bacterial DNA is still present in the nasopharynx. After the fourth week of cough, the amount of bacterial DNA rapidly diminishes which increases the risk of obtaining falsely-negative results.
- PCR testing following antibiotic therapy also can result in falsely-negative findings. The exact duration of positivity following antibiotic use is not well understood, but PCR testing after 5 days of antibiotic use is unlikely to be of benefit and is generally not recommended.

DO call the laboratory at 715-221-6700 or 800-222-5835 with any questions.

HOW TO ORDER BORDETELLA DETECTION BY PCR

Lab Test Code: BORDPCR

- COM: Bordetella by PCR
- Centricity: Bordetella by PCR
- DOWNTIME: Write-in (Form II)

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SPECIMEN

Submit one flexible wire shaft nasopharyngeal swab of Dacron or Rayon in Amies semi-solid gel with charcoal transport medium or 1 mL nasopharyngeal aspirate in a sterile container. A nasopharyngeal swab of Dacron or Rayon in a sterile container without media is also acceptable, but is not the preferred specimen transport. Calcium alginate is NOT acceptable for PCR. Separate swabs in separate transport media are needed if both culture and Bordetella by PCR are ordered. (See Culture, Bordetella for specimen requirements.)

STORAGE

Less than or equal to 24 hours at room temperature. Longer than 24 hours, refrigerate.

AVAILABLE

Test is performed Monday through Friday. During this high peak period, test is performed daily.
Analytical time:
24 hours.

QUALITATIVE INTERPRETATION

- Negative result
- Positive result
- Indeterminate with commentary recommending repeat testing if clinically indicated

CPT CODE

87801

INTERPRETIVE QUESTIONS CONTACT

Timothy Uphoff, PhD at 715-221-6700 or 800-222-5835.

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- Loeffelholz, M. (2012). "Towards Improved Accuracy of Bordetella pertussis Nucleic Acid Amplification Tests." Journal of Clinical Microbiology **50**(7): 2186-2190.
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- Leber A et al. Detection of Bordetella pertussis DNA in Acellular Vaccines and in Environmental Samples from Pediatric Physician Offices. 2010 Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC): Boston, USA.