UC Health LABORATORY

Lab Update

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In this issue:

LabUpdate is a periodic publication of the Clinical Laboratories of UC Health. By way of this publication, lab users are provided: 1) updated operational information relevant to the practice of laboratory medicine within UC Health facilities, and 2) didactic material generally applicable to laboratory medicine.

LAB UPDATE
University Hospital Clinical Laboratory

If you are interested in the on site availability of a particular test, please contact the Laboratory Client Services Department at 584-0696 or via email to Jenny Ford at jennifer.ford@uchealth.com.

MOLECULAR DIAGNOSTICS

Molecular Testing for Thrombotic Episodes

Current data shows that up to 50% of patients who present with a deep venous thrombosis have an underlying genetic predisposition for thrombosis. The two most common inherited conditions involve coagulation factors II and V. Factor V Leiden is a single base mutation (G1691A) that confers resistance to inactivation by protein C, an important regulator of the coagulation cascade. Prothrombin, also known as Factor II, can undergo a base pair mutation (G20210A) which results in increased production. Factor II is part of a complex that generates thrombin, which activates platelets and converts fibrinogen to fibrin. The fibrin meshwork forms the structure to which platelets adhere and form a clot.

Now available at UC Health Molecular Laboratory is a molecular test that can identify these two common mutations, Factor V Leiden and Factor II G20210A. The test is run on the Gene Xpert, which detects the targeted single base pair mutations by real-time polymerase chain reaction.

Due to the high sensitivity of the test, it is important that a dedicated tube be drawn for this testing in order to preventcontamination with extraneous DNA. The need for a pure DNA sample likewise prohibits this test from being ordered as an add-on. Either a sodium citrate or EDTA sample may be submitted. A refrigerated sample is stable up to 15 days. The turnaround time is 24 hours. Results are reported as normal, heterozygous (1 of 2 gene copies mutated) and homozygous (both gene copies mutated) for each mutation.

Since this test looks for a single base pair mutation in specific genes, individuals with other inherited risk factors such as abnormalities of protein C, protein S, or antithrombin will not be identified. These three factors combined are present in less than 1% of the general population, but in patients with thrombosis may reach 10%. Additionally, polymorphisms in DNA surrounding the genes of interest and/or substances that inhibit PCR may affect the ability to amplify DNA and could produce an invalid result. Any patient with a recent exposure to heparin should also be tested for heparin-induced thrombocytopenia. A patient with prolonged PT and/or PTT should also be tested for antiphospholipid antibodies. Additional laboratory abnormalities which may point to a cause include elevated factors VIII or XI and/or homocysteinemia.

Results of Factor V and Factor II testing should be interpreted in light of the patient's acquired risk factors or thrombosis, which include obesity, increased estrogenic states (pregnancy, OCP), immobilization, surgery, smoking, and malignancy. These risk factors are synergistic and together can increase risk to a greater extent than simply adding individual risk factors.

Factor V Leiden heterozygotes may comprise 3-5% of the population (most prevalent in Caucasians) and carry a 6-fold risk of venous thrombosis without additional risk factors. Heterozygotes for prothrombin G20210A may comprise up to 2% of the population and carry a 2-

risk factors, while homozygotes carry a 4-fold risk.

Lastword Order Descriptions:
Factor 5 Leiden and Factor 2 DNA

Questions regarding the interpretation of this test should be directed to Dr. Fred Lucas at 584-3840. Questions regarding performance of this test should be directed to Dr. Judith Rhodes at 584-3923.

Screening for Group B *Streptococcus*

The UC Health Microbiology and Molecular Laboratory is bringing screening for Group B *Streptococcus* (GBS) in house. The lab will be using a highly sensitive DNA amplification method to test for the presence of GBS in samples from pregnant women. The test will be performed daily, Mon – Sat, and the test code is SBDP. In most cases, the turnaround time for this test will be 24 – 48 hours. If culture and susceptibility testing are required, due to severe penicillin allergy (see below), an additional 48 – 72 hours may be needed to complete testing.

The Centers for Disease Control first issued guidelines for universal screening of pregnant women for GBS in 2002 as part of a nationwide strategy to prevent early-onset GBS disease. Approximately 10 – 30% of women are colonized with GBS, and colonized women are almost 25 times more likely to deliver infants with early-onset GBS disease. Thus, screening to identify GBS-colonized women is important, so that those women can be given intrapartum antibiotics.

Vaginal/rectal swab(s) from pregnant women between 35 and 37 weeks gestation should be submitted for testing. Most plastic shafted swabs, including eSwabs, can be used, as long as the transport medium does not contain charcoal.

In the 2010 update of the CDC Guidelines (MMWR 59:RR-10, 2010), the recommendations for laboratory testing were expanded to include newer nucleic acid amplification tests that had been developed since the previous publication. In their analysis, these molecular tests compared very favorably with traditional culture based methods. The procedure UC Health has adopted will use the recommended overnight broth enrichment prior to testing for the presence of DNA from GBS, also known as *Streptococcus agalactiae*. A sensitive isothermal amplification method called LAMP is used to detect the GBS DNA (illumingene® Group B *Streptococcus*). Numerous studies have shown that DNA amplification methods performed on enrichment broths have sensitivities and specificities between 93% and 100%, making them at least 10% more sensitive than culture based methods. Test results will be reported as Positive or Negative for GBS.

The guidelines call for pre-natal treatment of colonized women with penicillin or ampicillin. Because GBS isolates are predictably susceptible to penicillin and ampicillin, it is not necessary for the lab to grow the organism for susceptibility testing. In women with a history of severe allergic reaction to penicillin (anaphylaxis, angioedema, etc.), physicians may contact the lab for susceptibility testing for clindamycin, the recommended second line agent. On occasion, due to the higher sensitivity of the DNA amplification test when compared with culture, it may not be possible to isolate viable GBS for further testing. However, in most cases, isolation, identification and testing for susceptibility or resistance to clindamycin, including induced resistance, will be performed and reported in the next 48-72 hours. If you have any questions about laboratory testing for Group B *Streptococcus*, please contact Dr. Rhodes at 584-3923 or Vicki Stegner at 584-6014.

TRANSFUSION MEDICINE

Transfusion-Transmitted Disease
Reminder to Physicians:

Physicians are reminded that it is possible to transmit disease via blood transfusion. Transfusion-transmitted diseases may include but are not limited to HIV, hepatitis B, hepatitis C, West Nile virus, human T lymphotopic virus (HTLV I / II), CMV, malaria, babesiosis, syphilis, Chagas' disease, toxoplasmosis, and Lyme disease. The physician notifies the Blood Bank when a patient develops a change or diagnosis suggestive of a transfusion-transmitted disease. Changes would include unexplained acute liver dysfunction or changing serology occurring 2 weeks to 12 months after transfusion. For West Nile Virus, the transfusion must have occurred within 28 days of developing the illness.

UC Health Blood Bank can be notified at 513-584-7888. Information provided to the blood bank should include the patient's name, medical record number or birth date, and type of transmitted disease suspected.