

**March 2017**

## New Meningitis/Encephalitis PCR Panel

Central nervous system infections may be caused by a variety of micro-organisms, most commonly bacteria, viruses, or yeast. Mortality from these infections is high (15%) as is the risk for long-term sequelae such as loss of motor function, visual and hearing deficits, and seizures.

Saint Luke's Microbiology now offers a multiplex PCR for rapid detection of 14 central nervous system pathogens.

<b>Organisms detected by CSF panel</b>
<b>Escherichia coli K1 subtype</b>
<b>Haemophilus influenza</b>
<b>Listeria monocytogenes</b>
<b>Neisseria meningitidis</b>
<b>Streptococcus agalactiae</b>
<b>Streptococcus pneumonia</b>
<b>Cytomegalovirus</b>
<b>Enterovirus</b>
<b>Herpes simplex virus 1</b>
<b>Herpes simplex virus 2</b>
<b>Human herpesvirus 6</b>
<b>Human parechovirus</b>
<b>Varicella zoster virus</b>
<b>Cryptococcus neoformans/gattii</b>

Performance characteristics include an overall sensitivity and specificity of 94.2% and 99.8% respectively. This panel provides accurate and rapid detection of the most common pathogens associated with meningitis and encephalitis, however it does NOT replace cerebrospinal fluid (CSF) bacterial culture and Gram stain. Likewise,

Cryptococcal antigen and fungal culture should be ordered in addition to the panel in patients at risk for this infection.

This panel is orderable as 'CSF Panel' and specimen requirement is 1mL of unspun CSF collected by lumbar puncture. CSF specimens from shunts or other central nervous system devices are not suitable for testing.

## Clinical Practice Guidelines for Red Blood Cell Transfusion

AABB recently published the clinical practice guidelines for red blood cell (RBC) transfusion (JAMA 2016;316(19):2025-2035). These guidelines are based on research in RBC transfusion medicine which has significantly advanced the science in recent years and provided high-quality evidence.

A restrictive transfusion threshold has been suggested to be safe in most clinical settings. Resonating with the AABB guidelines, SLHS is updating the RBC transfusion indication(s):

- Hgb less than or equal to 7g/dL and symptomatic anemia in hemodynamically stable patients, including critically ill patients
- Hgb less than or equal to 8 g/dL and symptomatic anemia in patients with underlying cardiovascular disease or undergoing orthopedic surgery or cardiac surgery
- Acute massive blood loss not corrected by volume resuscitation
- Red cell exchange (sickle cell disease)

In emergent trauma and operating room bleeding, clinicians also have the option to use the massive transfusion protocol. Neonatal/pediatric transfusions were not included in these guidelines but symptomatic anemia and exchange transfusions are the most common indications for RBC transfusions.

In addition, it has been strongly recommended that the current blood banking practice of using standard-issue blood (fresher blood does not improve clinical outcomes) should be continued for all patient populations (including neonates).

The JAMA Clinical Guidelines Synopsis (JAMA 2016;316(19):2038-2039) also suggested considering single-unit transfusions for patients without active bleeding. Clinically reassessing and checking hemoglobin levels after each single-unit transfusion to decide if further transfusions are needed is recommended.

### **Testosterone-Replacement Therapy – A Factor in Thromboembolic Event?**

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In the United States, the estimated number of men older than 40 years taking some form of testosterone-replacement therapy has steadily increased over years (2.9% of all men over 40 years in 2011). A “Perspective” article published in New England Journal of Medicine, 2015 concluded that “to date there is no definite evidence that increasing serum testosterone concentrations in men (with age-related hypogonadism) is beneficial and safe” (Nguyen CP, et. al. N Engl J Med. 2015;373:689-691). An inconclusive but possible prothrombotic effect in patients on testosterone replacement therapy has brought safety into question. It is unclear whether testosterone is prothrombotic per se, or only observed in patients who experience testosterone-induced erythrocytosis.

These issues are important especially in patients who develop a venous thromboembolic event (VTE) while on testosterone-replacement therapy and also in patients with history of VTE who are

considering testosterone-replacement therapy. A recent study performed on a very large population in the United Kingdom reported, adjusted rate ratio of VTE near 1.25 (95% CI, 0.94 -1.66) for current versus no testosterone therapy. During the first six-months of testosterone therapy, the rate ratio of VTE reported was 1.63 (95% CI, 1.12 - 2.37), which following longer therapy decreased to 1.00 (95% CI, 0.68 – 1.47). In this study route of administration (intramuscular, transdermal and oral) yielded similar rate ratio. The conclusion of this study was that initiation of testosterone therapy is associated with increased risk of VTE, which peaked at six months and decreased, thereafter (Martinez C. BMJ. 2016;355:i5968).

Based on these data, in patients presenting with thromboembolic event, testosterone-replacement therapy, especially if initiated recently (less than six months), should be considered as one of the potential causes.

### **New scoring system to diagnose TTP**

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Thrombotic thrombocytopenic purpura (TTP) is a severe life threatening disease characterized by thrombotic microangiopathy. It is caused by lack of ADAMTS13 activity, which cleaves the von Willebrand factor. Researchers at Massachusetts General Hospital developed a new scoring system, “PLASMIC score”, to predict ADAMTS13 deficiency (*Derivation and external validation of the PLASMIC score for rapid assessment of adults with thrombotic microangiopathies: a cohort study*. The Lancet Haematology.2017).

Five independent variables including platelet count  $<30 \times 10^9/L$ , creatinine  $<2.0mg/dL$ , INR  $<1.5$ , MCV  $<90$  fL, and hemolysis were identified to be highly predictive. Cancer history and hematopoietic stem cell transplant or solid-organ transplant were also included in the model because of their high negative predictive value. The PLASMIC scoring system was validated in two different cohorts, and when used in conjunction with clinical evaluation may help to quickly diagnose new TTP patients.