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Blood Transfusions & Risk of VTE

Venous thromboembolism (VTE) is a major cause of morbidity and mortality (5-10% of hospital deaths) in hospitalized patients. The most common presentations of VTE are deep vein thrombosis (DVT) of the lower extremity and pulmonary embolism (PE). It is estimated that over half of hospitalized medical patients are at risk for VTE. Moreover, about 70% of hospital-acquired VTE are preventable. The US Centers for Medicare & Medicaid Services (CMS) has added VTE during admission for certain surgical procedures to the list of "never events". If a patient develops VTE following one of these procedures, a portion of the payment made by CMS to hospitals is to be withheld.

The major acquired risk factors for VTE include prior thromboembolism, recent major surgery, trauma, immobilization, antiphospholipid antibodies, malignancy, pregnancy, oral contraceptives, and myeloproliferative disorders. VTE prophylaxis includes early ambulation, mechanical methods (eg, intermittent pneumatic compression, graduated compression stockings, or venous foot pump), and pharmacologic thromboprophylaxis (low molecular weight heparin, unfractionated heparin, or fondaparinux).

Perioperative red blood cell (RBC) transfusions have also been postulated to potentiate the postoperative prothrombotic state. Results of recently published research (doi:10.1001/jamasurg.2018.1565) suggest that perioperative RBC transfusions may be significantly associated with the development of new or progressive postoperative VTE within 30 days of surgery, independent of several putative confounders.

Investigators analyzed data, from the American College of Surgery National Surgical Quality Improvement Program (ACS-NSQIP) database, for patients who underwent a surgical procedure between Jan. 1 and Dec. 31, 2014. The study

included 750,937 patients, of whom 47,410 (6.3%) received at least one perioperative RBC transfusion. Of these, 3,605 (0.5%) received only perioperative RBC transfusion, while 40,015 (5.3%) received only intraoperative or postoperative RBC transfusions. A total of 3,790 patients received both preoperative and intraoperative or postoperative RBC transfusions.

Postoperative VTE occurred in 6,309 patients (0.8%) (DVT in 4336 [0.6%]; PE in 2514 [0.3%]; both DVT & PE in 541 [0.1%]). Perioperative RBC transfusion was associated with higher odds of VTE (aOR, 2.1; 95%CI, 2.0-2.3), DVT (aOR, 2.2; 95%CI, 2.1-2.4), and PE (aOR, 1.9; 95%CI, 1.7-2.1), independent of various putative risk factors. Furthermore, a significant dose-response effect was observed with increased odds of VTE as the number of intraoperative and/or postoperative RBC transfusion events increased (aOR, 2.1 [95%CI, 2.0-2.3] for 1 event; 3.1 [95%CI, 1.7-5.7] for 2 events; and 4.5 [95%CI, 1.0-19.4] for 3 events vs no intraoperative or postoperative RBC transfusion; $P < .001$ for trend).

Results of this study add to the growing evidence for utilizing patient blood management principles while transfusion patients i.e. to transfuse patients only when needed, and not just in case.

***Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG) PCR Order Change**

Due to a change in test codes, effective 7/18/18, urine and swab samples for CT/NG PCR will now have separate orders for each. Epic lab order options and preference list choices are: CTNG PCR Urine, CTNG PCR Swab, CT PCR Urine, CT PCR Swab, NG PCR Urine, and NG PCR Swab.

There is also a slight change to the preferred collection kit for CT and/or NG PCR swab testing. The new kit is the Roche Cobas PCR Uni Swab Sample Kit, which contains transport media and a single polyester woven swab. These kits will continue to be available by the current process and

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any remaining old collection kits may still be used. Please contact the Molecular Diagnostics Laboratory at 816-932-3886, or Saint Luke's Regional Laboratories Client Services at 816-932-3850 to request collection kits.

Test methodology and performance characteristics are unchanged. Saint Luke's Molecular Diagnostics performs CT and NG PCR by Roche Cobas 4800. Preferred samples are an endocervical swab for women, and first-catch urine for men. Testing is done daily Monday through Friday.

Chlamydia trachomatis is the most common bacterial sexually transmitted disease in the United States with more than 1 million infections reported annually. As many as half of infections are believed to be asymptomatic, with many undetected and untreated. Serious complications of infection include infertility and ectopic pregnancies. Infants born to infected women can develop conjunctivitis, pharyngitis, and pneumonia. Likewise, many *Neisseria gonorrhoeae* infections in women are asymptomatic, and occur as co-infections with CT, *Trichomonas vaginalis*, and bacterial vaginosis. Complications of NG infection include pelvic inflammatory disease, endometritis, salpingitis, tubo-ovarian abscess, peritonitis and perhepatitis.

Sensitivity and specificity for CT/NG PCR tests are 95% or greater, with minor differences between specimen types. Testing of endocervical swab and urine specimens have slightly better yield than vaginal swab and PAP smear specimens. The Roche Cobas 4800 assay detects both wild-type and variant DR-9 sequences of NG and all fifteen major CT serovars.

Laboratory Testing in Hereditary Hemochromatosis

Hereditary Hemochromatosis, the most common inherited genetic disorder in European populations, can result from mutations in HFE gene and non-HFE genes. Individuals homozygous for the most common mutation in HFE gene leading to the p.Cys282Tyr substitution, may develop iron overload and its clinical consequence depending on other contributing co-factors including environmental factors, gender, alcohol consumption, and blood loss. The main mechanism whereby iron exerts its deleterious effects is the generation of reactive oxygen species, which in turn increase lipid peroxidation, resulting in damage to organelles and DNA.

Hemochromatosis is classified into:

1. Type 1 (HFE-related)
 - a. Type 1a: Cys82Tyr homozygosity
 - b. Type 1b: Compound Cys82Tyr/His63Asp heterozygosity
 - c. Type 1c: Other HFE genotypes (Ser65Cys, etc)
2. Type 2 (non-HFE-related)
 - a. Type 2a: Juvenile hemochromatosis (hemojuvelin mutations)
 - b. Type 2b: Juvenile hemochromatosis (hepcidin mutations)
3. Type 3 (Mutated transferrin receptor 2)
4. Type 4 (Mutate ferroportin 1 gene, SLC11A3)

Individuals with p.Cys282Tyr homozygosity may present with abnormal iron studies such as increased serum ferritin levels. Due to low specificity of serum ferritin levels, such individuals may or may not have clinical symptoms or proven evidence of iron overload. However, a normal serum ferritin level at diagnosis is unlikely to be associated with symptomatic disease. The most common presenting features of hemochromatosis include chronic fatigue, arthropathy, and bone disease. Other iron related tests including serum iron concentration and percentage saturation of transferrin have better specificity than serum ferritin levels. A persistent fasting serum transferrin saturation of more than 45% is an early sign of hemochromatosis and should be followed by HFE testing. Other HFE genotypes including compound (p.Cys282Tyr/His63Asp) may show increased transferrin saturation and serum ferritin levels, however usually are not associated with iron overload-related disease.

A recent study performed at Danbury Hospital, Danbury, CT developed an algorithm criteria for HFE gene testing, which required either presence of transferrin saturation of >45% or a family history of hereditary hemochromatosis. The study observed an overall decrease in HFE gene testing with no statistically significant decrease in clinically significant HFE genotypes, thereby preventing over- or mis-utilization of HFE gene testing.

At Saint Luke's Molecular Diagnostics, hemochromatosis genotype (including C282Y and H63A) testing is performed on whole blood (EDTA/lavender or sodium citrate/light blue tube), once per week. The tests should be preferably requested on individuals with transferrin saturation >45% or presence of family history.